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## DESCENDING MESENCEPHALIC TRACTS IN CAT, MONKEY AND MAN; MONAKOW'S BUNDLE; THE DORSAL LONGITUDINAL BUNDLE; THE VENTRAL LONGITUDINAL BUNDLE; THE PONTO-SPINAL TRACTS, LATERAL AND VENTRAL; THE VESTIBULO-SPINAL TRACT; THE CENTRAL TEGMENTAL TRACT (CENTRALE HAUBENBAHN); DESCENDING FIBRES OF THE FILLET.

(*The tracts from the nuclei fastigii to Deiters's nuclei; descending thalamo-spinal fibres; a tract from the inferior collicular region to the ventral column of the spinal cord.*)


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In the course of an experimental research upon the paths subserving certain reflex phenomena in the central nervous system of the cat and monkey carried out at the Laboratory of Pathological Chemistry, University College, London, under a license held by one of us (J.C.), we had occasion to make certain lesions of the mesencephalon.

The degenerations resulting from some of these experiments are here recorded. A series of cases in which destruction of the quadrigeminal and upper pontine region had occurred as a result of new growth or softening have been recently examined by us in the Pathological Laboratory of the National Hospital, and have given us the opportunity of comparing the experimental degenerations in the cat and monkey with those resulting from disease of the same region in man.

Our best thanks are due to Professor Vaughan Harley for kind permission to use his laboratory at University College, to Professor Victor Horsley for valuable criticisms and suggestions, and to the Medical Staff of the National Hospital for permission to make use of their cases. Dr. Newton Pitt most kindly sent us the case of mesencephalic abscess from Guy's Hospital. (This case will shortly be published by him in detail.)

## Methods.

The lesions of the mesencephalon were made by removing an area of bone over the posterior part of the sagittal suture, gently separating the hemispheres and puncturing through the corpus callosum with a cataract knife, without exposing the lamina quadrigemina. In every case the wounds healed by first intention. The animals were killed with an overdose of chloroform from fourteen to twenty-one days after operation. Both the experimental and pathological tissues were removed as soon as possible after death and were hardened in formalin for twenty-four to seventy-two hours and subsequently in Muller's fluid for eight days. For the Marchi method Bouche's sodium iodate modification was used, and for staining the medullated fibres Robertson's copper pyrogallic method and the Kulchitsky-Wolters method. The sections were cut in celloidin and mounted in serials.

The line diagrams were traced from the specimens by means of Edinger's apparatus, and the photographs were made with the same apparatus.

## Nomenclature.

Since some of the tracts dealt with in this communication have been described by authors under many different names, it will be convenient here to indicate these names and to add a brief anatomical description of each tract according to the most recent German investigators. We have adopted the terminology by which these tracts are referred to in recent French and German indexes.

*Monakow's bundle.—Vierhügel-seitenstrangbahn; Abirrendes Seitenstrang-bündel (Monakow); Rubro-spinal tract (Pavlow); Le faisceau mésencephalo-spinale croisé laterale; Boyce's tract; Aussere Seitenstrang-bündel (Meynert); Fibres fondamentales du cordon lateral; Faisceau pré-pyramidal (Thomas, in the cord); Fasciculus tecto-spinalis cruciatus (Edinger); Lateral columnar tract (Boyce).*

This tract was probably seen by Forel in 1884 in the mesencephalon and pons, but it was not traced to the spinal cord. It was first described by von Monakow in 1883, after hemisection of the cord below the pyramidal crossing in the dog, and subsequently after section of the lateral fillet at the level of the issuing fifth nerve. The development of the tract was investigated by von Bechterew and Held and more recently by Hösel; the fibres acquire their myelin early in the fifth month of fœtal life. The origin of the fibres in the red nucleus was ascertained by Held and Probst. Bechterew considers its place of origin to be the deep gray matter of the superior colliculus. The termination of the fibres among the cells of the ventral and dorsal horns of the spinal cord was shown by Probst and Rothmann.

This tract was investigated in birds by Münzner and Wiener and has been found constantly present in the rat, hedgehog, rabbit, guinea-pig, cat, dog and monkey. It was first described in man by Held.

The tract is composed of large fibres which arise in the cells of the red nucleus and issuing from its mesial aspect

lie in a bundle immediately ventro-mesial to that structure. They cross the middle line sharply, decussating with those of the opposite side between the roots of the oculo-motorius in Forel's crossway—that part of the tegmental decussation lying between the fountain crossway of Meynert and the crossing of the brachium conjunctivum. The tract then turns caudalwards lying dorsal to the substantia nigra, ventro-mesial to the caudal end of the red nucleus and external to the issuing roots of the oculo-motorius. It then passes on to the dorsal aspect of the mesial fillet and gradually passing over this structure from within out, sinks through the angle of junction of the mesial and lateral fillet at the level of the motor nucleus of the fifth nerve and comes in relation with the mesial aspect of the spinal root of the fifth nerve. At the level of the exit of the seventh nerve the tract lies lateral to the superior olive, ventro-mesial to the spinal root of the fifth nerve and reaches the surface of the medulla crossed by fibres of the issuing seventh nerve. Below this it occupies the dorsal part of the fasciculus lateralis proprius of the medulla, lies immediately ventral to the spinal root of the fifth nerve and is mixed with the fibres of the lateral ponto-spinal tracts, the vestibulo-spinal tract and Gowers' bundle.

In the cervical cord the fibres are scattered over a wedge-shaped area with the base ventral and lateral, stretching from the mesial aspect of Gowers' bundle to the middle of the dorsal horn. The fibres which are traceable to the sacral region blend with the lateral pyramid below the cervical region and end among the cells of the ventral horn and in lesser extent also of the dorsal horns.

Contained also in Monakow's bundle are fibres which degenerate above points of section and are said to connect the ventral horn of the spinal cord with the nucleus ruber.

*The dorsal or posterior longitudinal bundle* needs no special description in this communication.

*The ventral longitudinal bundle.—Vierhügelvorderstrangbahn ; Prædorsales Längs bündel (Tschermak) ; Faisceau*

*long. prédorsal ; Faisceau tecto-bulbaire (Pavlow) ; Faisceau marginale descendant ; Systéme du zone sulcomarginal (Marie) ; Fibres fundamentales des cordons antérieures (Hösel).*

This tract was first described by Held in 1892. The most important investigations and descriptions are those of Held, Tschermak, Pavlow, Boyce, Rothmann and Probst. Hösel has investigated the tract developmentally and has found that myelination of the fibres takes place in man during the fourth month of fœtal life shortly after that of the dorsal longitudinal bundle and before any other fibres than those of these two systems are medullated in the ponto-bulbar region.

These fibres have their origin in the deep gray matter of the superior colliculus close to the gray matter surrounding the aqueduct ; they course ventralwards and caudalwards to cross the middle line in Meynert's fountain crossway and then lie in a distinct bundle ventro-lateral to the dorsal longitudinal bundle, the distance between these two tracts increasing as they course down to the medulla where they come together and run into the anterior column of the cord. Collaterals leave the fibres of the ventral longitudinal bundle to end in the lateral stratum griseum centrale, in the lateral and contra-lateral oculo-motor nuclei and in the contra-lateral nucleus trochlearis and nucleus abducentis. The tract becomes much reduced in size below the nucleus abducens and can be traced in the anterior column of the cord as far as the lower lumbar region lying along the ventral border of the anterior fissure. The fibres terminate among the cells of the ventral horn some passing across the ventral commissure to end in the opposite ventral horn. The ventral longitudinal bundle consists entirely of fibres which degenerate downwards (Probst).

Held has described fibres running in the v. l. b. which, taking their origin from cells of the deep gray matter of the superior colliculus just behind the nucleus commissuræ dorsalis, run directly into the v. l. b. of the same side. (Ungekreutz Vierhügel-vorderstrangbahn).

*The Ponto-spinal tracts.*[1] — *Brücke-seitenstrangbahn Brückevorderstrangbahn; Fissurenstrang (Tschermak); Ungekreutzes Pyramidseitenstrang-system; Gekreuztes absteigendes Syst. aus dem mittl. und unteren Centralkern; Vorderseitenstrangreste der Mittelline (Held).*

These tracts were discovered and their origin and connections with the spinal cord partly described by von Bechterew using the myelination method in 1885. A good collective description of them is given by this author in the last edition of his treatise. Another excellent description is that of Tschermak. Fusari has described the tracts in man, degenerate after morbid lesions of the brain stem.

Separated as a crossed and an uncrossed system these fibres descend into the cord from the large cells of the reticular formation scattered from the medulla to the colliculus inferior, especially the nuclei centralis medius and lateralis medius of Bechterew and the central and lateral nuclei of Flechsig.

The mesial uncrossed system (Vorderseitenstrang-restes der Mittellinie of Held) runs into the dorsal longitudinal bundle, and can be traced as low as the conus teminalis occupying the borders of the ventral fissure (Fissurenstrang of Tschermak). They give many collaterals to the reticular formation of the medulla and others to end in the ventral horns of the spinal cord. (Uncrossed descending spinal nervous system from the reticular formation (Barker), Brucke-vorderstranghbahn of Bechterew.)

The crossed lateral system (Brucke-seitenstrangbahn of Bechterew) has its origin chiefly in cells of the nucleus centralis medius of Bechterew by fibres which immediately cross the middle line, and coursing through the d. l. b., turn caudally to lie between the d. l. b. and the inner limb of the facial; they then edge out into the olivo-restiform angle lying between the nucleus lateralis and spinal fifth, and run in the fasciculus proprius lateralis throughout the length of the spinal cord. In the cord the fibres lie

[1] No name having been applied to these tracts in English, we venture to use this term as equivalent to the German Brücke-seitenstrangbahn and Brucke-vorderstrangbahn.

somewhat scattered in the dorso-lateral part of the lateral pyramidal field, mesial to the fibres of Monakow's bundle and Gowers' bundle. They are said to terminate in the central region of the gray matter.

*The vestibulo-spinal tract.—The descending tract from Deiters's nucleus; Absteigende Kleinhirnbahn (Biedl).*

This tract consists of large fibres which have their origin in the cells of Deiters's nucleus, and also in the cells of the upper vestibular nucleus of von Bechterew. From these nuclei they take a curved course ventro-mesially, and crossing the facial knee sink to the mesial side of the facial nucleus and enter the fasciculus proprius lateralis medullaris. The fibres are mixed with those of Monakow's bundle, the ponto-spinal descending tracts, the antero-lateral spino-thalamic fibres and those of Gowers' bundle. The vestibulo-spinal fibres occupy however chiefly the mesial aspect of this region. In the lower medulla the tract lies between the nucleus lateralis and the remains of the anterior horn. In the spinal cord they lie in the anterior root zone and extend to the ventro-mesial angle of the ventral horn. They can be traced to the lower lumbar cord ending in the ventral horn of the same side.

This tract was first described by Held in 1890, and has been developmentally studied by Obersteiner. These authors gave the origin of the tract as above described. Marchi, Biedl, Basilewsky and others found this tract degenerate after hemi-extirpation of the cerebellum, and referred its origin to that organ. Russell showed that such degeneration subsequent to cerebellar hemi-extirpation was due to the coincident damage to Deiters's nucleus, and many writers have since confirmed this view.

*The central tegmental tract.—Fasciculus tegmenti centralis (Barker); Centrale-Haubenbahn (von Bechterew) (Flechsig).*

This tract was first described by von Bechterew, and subsequently by Flechsig. The former has recently investigated

degeneration of this tract in man. It is one of the latest of all tracts to acquire myelin and for this reason is easily studied during development. It is a descending tract, but its origin, probably thalamic, has not been definitely ascertained. At the region of exit of the oculo-motorii it is fusiform in section and lies mesial to the nucleus ruber and outside the roots of the third nerve. At the level of the exit of the fifth nerve its position is quite central in each lateral half of the tegmentum; hence its name. The tract then drops ventralwards as it descends, and comes to lie between the inferior olive and the fasciculus lateralis proprius medullæ. Bechterew is alone in stating that it is continued below the olive as the olivenstrang (Dreikentenbahn of Helweg). "Abwärts scheint sich die Centrale Haubenbahn in der Olivenstrang des Ruckenmarks fortzusetzen." Other writers, however, deny the unity of the Centrale Haubenbahn with this triangular field.[1]

*Descending fibres of the fillet.—Accessorische Schleife (Bechterew); Lateral pontine bundle (Schlesinger).*

Very little that is definite can be found in neurological literature as regards centrifugal fibres in the mesial fillet. That certain of its fibres acquire their myelin late (after birth) suggesting centrifugal function has long been known through the researches of Flechsig and von Bechterew.

Hoche has described fibres in two cases in man which seem to have a definite course (the cases were thrombotic hemispheric lesions). The fibres left the capsule and occupied a position in the crus immediately lateral to the pyramidal fibres. In the pons they leave relation with the pyramidal fibres and coursing in a dorsal and mesial direction run caudalwards in the middle fillet whence some of the fibres pass to the nucleus facialis of the same and opposite side; other fibres enter the interolivary layer and course to the nuclei hypoglossi of the same and opposite side. Many other observers have noticed descending degeneration in the

[1] In a recent publication Bechterew has, however, stated that the triangular tract arises on the surface of the inferior olive as the fasciculus peri-olivaris.

mesial fillet, but the course of the fibres has not been definitely traced.

In both monkey and man lesions of the quadrigeminal region have produced atrophy of the fillet and inferior olive on the side of the lesion, but only after some time. It is difficult to distinguish such secondary atrophy from primary degeneration in pathological lesions when death occurs after the lapse of a considerable time.

## Experimental Degenerations.

*Experiment* 1.—Cat. Lesion on either side of the middle line dividing the posterior half of the dorsal commissure, the fountain crossway and part of Forel's crossway; the habenular commissure was not divided.

Descending degeneration in both Monakow's bundles R. > L., both dorsal longitudinal bundles L. > R., the right ventral longitudinal bundle. (Plate I.—V.)

The lesion was produced in an attempt to divide the ventral part of the dorsal commissure, the fine cataract knife being introduced in the middle line with the cutting edge directed caudally, and the handle inclined strongly forwards. By an accidental movement of the knife a double linear lesion resulted, cutting a piece out of the posterior half of the dorsal commissure and running deeply on either side of the aqueduct along the mesial aspects of the caudal extremity of the red nuclei. On the left side the line of section extended to the interpeduncular space, on the right side to a point midway between the aqueduct and ventral surface of the mesencephalon lateral to the mid-line. The nuclei of the oculo-motorius and radix descendens trigemini were apparently not injured, each lesion lying external to the first and internal to the second, for there was no degeneration of the corresponding root fibres. The lesion did not involve the nuclei trochleares. The lesions were very sharply limited; there had been apparently little or no hæmorrhage.

In front of the lesion degenerate fibres were seen crossing in the lower part of the intact anterior half of the dorsal commissure to end in the nucleus commissurae dorsalis. On

either side degenerate fibres ran forwards from the lesion to end in the gray matter along the sides of the third ventricle. The left fasciculus pedunculo-mamillaris was degenerate. The fasciculus retroflexus of Meynert was not degenerate. No degeneration was seen in the optic tracts, but a few fibres of the posterior commissure entered the external geniculate body on both sides.

Lateral to the lesions a few fibres passed outwards to end in the nucleus centralis superior. Ventral to the aqueduct no degenerate fibres were seen crossing the mid-line in front of the level of the exit of the anterior fibres of the oculomotorius.

From the cut ends of the dorsal commissure many degenerate fibres were seen coursing to the nucleus cent. sup. and nucleus com. dorsalis and many fibres to the dorsal longitudinal bundles on both sides. Fibres could be traced from the dorsal commissure to the ventral longitudinal bundle without any decussation below the aqueduct. Behind these, fibres from the nucleus lat. superior and deep gray matter of the superior colliculus crossed in Meynert's decussation and apparently passed into Monakow's bundle and the v.l.b. of the other side. No fibres were traced from dorsal commissure to the nucleus ruber.

A few of the anterior rootlets of the outgoing oculomotorius were degenerate, but only the first two sections showing these contained degenerate fibres.

In this region there was little or no degeneration in Meynert's fountain crossway, but in Forel's crossway, between the roots of the third nerve, were very many thick degenerate fibres forming apparently a complete decussation. These fibres commenced where the linear lesion skirted the mesial aspect of the caudal extremity of the nucleus ruber. The fibres crossing from right to left were not so plentiful as were those crossing in the opposite direction (the lesion did not extend so far ventral on the right side). Having crossed the roots of the third nerve, these fibres turned caudalwards and lay dorsal to the mesial end of substantia nigra, just outside the third roots, forming two conspicuous bundles—Monakow's bundles, the right con-

taining twice as many fibres as the left, that is, in crossed relation to the more extensive lesion near the left red nucleus. In the region of the inferior colliculus these tracts passed on to the dorsal aspect of the mesial fillet and, edging outward in their course, came in relation with the mesial aspect of the spinal root of the fifth nerve, and passing to its ventral aspect maintained this position as low as the second cervical segment. At the level of the exit of the seventh nerve the tracts had a characteristic position, lying ventro-mesial to the spinal fifth, immediately external to the superior olive, and separated from the surface of the medulla by the fibres of the trapezium. In the lower medulla the fibres became somewhat separated and lay in the dorsal part of the fasciculus lateralis proprius, but some fibres came right down to lie immediately dorsal to the inferior olive. In the cervical cord the fibres occupied a fusiform area stretching from the mesial side of Gowers' bundle to the middle of the dorsal horn, and caudal of this region they were in the position of the lateral pyramidal tracts and were traced to the lowest sacral region.

Fibres leaving the tract in the medulla ran external to the spinal fifth and, passing through the restiform body, ended in the inferior vermis.

The termination of the fibres in the ventral and lateral horns was easily seen.

The dorsal longitudinal bundles contained many degenerate fibres, which occupied the dorsal and mesial parts of each bundle. These fibres were traced from the dorsal commissure. No fibres were traced across the fountain crossway (the lesions were outside the nucleus oculomotorius). The degenerate fibres were large and the left d.l.b. much more degenerate than the right. The tracts diminished in size considerably in the region of the sixth nucleus and in the cervical region. They were traced to the lower sacral region.

*Comments.*—The crossing and course of Monakow's bundles were typical. The position of the lesion mesial to the ventral end of the red nucleus more extensive on the left side, coupled with the greater degeneration of the right

bundle, suggests the exit of the fibres from the ventral end of the red nucleus. The origin of some of the fibres appeared to be in the deep gray matter of the superior collicular region, an origin which Held and Boyce suggested.

The crossed relation of the degeneration of the d.l.b. and v.l.b. was striking.

Most of the fibres of the right v.l.b. seemed to come from the region of the posterior commissure, and since the tract was degenerated upon the right side only, it is possible that they had their origin in the gray matter close to that structure and correspond to Held's description of the non-crossing ventral colliculo-spinal tract. The passage of fibres from Monakow's bundle by the inferior peduncle to the cerebellum has not, so far as we are aware, been hitherto noticed.

It is worthy of note that notwithstanding the position of the lesion the "Centrale Haubenbahn" was not degenerated.

*Experiment* 2.—Cat. Sagittal linear lesion upon the right side, extending from caudal end of soft commissure to a point opposite the centre of the superior colliculus; it extended vertically from the ventral limit of the aqueduct to the inter-peduncular space lying immediately mesial to the right red nucleus.

Degenerations below the lesion in the right dorsal longitudinal bundle, left ventral longitudinal bundle, and left Monakow's bundle. Fibres crossing in dorsal commissure to the ventral longitudinal bundle. (Plate VI.—VII.)

The lesion was produced in an attempt to cut the ventral fibres of the dorsal commissure, the knife introduced vertically in front of that commissure was tilted with the cutting edge back, so that the lesion produced was most extensive at its ventral limit, and viewed laterally was triangular in shape with the apex at the place of entry of the knife into the thalamus forward of the dorsal commissure on the left side and the base extending from the soft commissure into the region of Forel's decussation.

Some injury to the posterior part of the hemisphere on

the left side caused degeneration of the left optic radiation running into the left superior colliculus, and slight degeneration of the left pyramidal tract.

In front of the lesion the fasciculus retroflexus of the right side showed some degeneration and a good many fibres ran forwards to end in the gray matter lining the third ventricle on the right side, a few crossing to the opposite side in Meynert's commissure.

From the outer side of the lesion many fibres crossed in the dorsal commissure and ran caudalwards along the lateral limit of the central gray matter on the left side, many fibres being traceable into the nucleus centralis superior, while fibres in a similar position ran caudalwards on the right side.

Those on the side for the most part ended in the nucleus oculo-motorius, nucleus trochlearis and nucleus fasc. long. dorsalis of the left side but some coursed ventro-mesially and ran throughout the brain stem as fibres of the left ventral longitudinal bundle. Those on the right side entered the posterior longitudinal bundle and were traceable as far as the sacral region of the spinal cord, occupying the most dorsal limit of the anterior column against the white commissure. From the inner side of the lesion in the neighbourhood of the right red nucleus coarse fibres crossed in Forel's decussation to occupy the position of Monakow's bundle on the left side, this tract being in every way similar to those described in the experiment 3. They were traceable as far as the lower cervical region, below which they were indistinguishable from the fibres of the pyramidal degeneration.

The fibres degenerate in the right posterior longitudinal bundle occupied its dorso-mesial aspect. The degenerate fibres of the left ventral longitudinal bundle had the typical course described on p. 181. They were very large fibres always somewhat scattered and, becoming much reduced in numbers in the region of the sixth nucleus and still further in the medulla, were traced to the lumbar region occupying the ventral border of the anterior median fissure.

The oculo-motor and trochlear nerve-roots, the left d.l.b., right v.l.b. and right Monakow's bundle showed no trace of degeneration.

*Comments.*—The course of Monakow's bundle was typical and the absence of degeneration in the right bundle points to its fibres being entirely crossed.

The crossed relation of the degeneration of the d.l.b. and v.l.b. was again striking.

The degenerate fibres of the v.l.b. presumably came from the central gray matter close to the dorsal commissure as in the last case. This is in agreement with Held's results. The absence of degeneration in the "centrale Haubenbahn" is striking for it is difficult to conceive that it escaped injury on either side.

*Experiment* 3.—Rhoesus Monkey. Lesion in right superior colliculus and passing obliquely caudalwards, ventralwards and to the left, dividing Meynert's and in part Forel's decussation, damaging the nuclei oculo-motorii and trochleares and left red nucleus.

Degeneration below the lesion in both Monakow's bundles R. > L. reaching throughout spinal cord; right radix descendens trigemini, R. and L. dorsal longitudinal bundles and R. and L. ventral longitudinal bundles, and in both third and fourth nerves. (Plate VIII.—XII.)

The lesion was produced in the attempt to divide supposed fibres coming into the R. oculo-motor nucleus from the midthalamic region. A puncture, intended to be vertical with the blade of the knife transverse to the lines of the brain stem and a slight cut to the right, was made. The lesion was linear, transverse and localised. Roughly triangular in transverse section with apex above it extended from the centre of the R. sup. colliculus on its dorsal surface to the outer side of the left red nucleus crossing, the R. side of the central gray matter, touching the aqueduct at its ventral border, involving both third nuclei, both fourth nuclei, the left red nucleus and crossing Meynert's and Forel's decussations transversely, did not extend ventrally into the substantia nigra. The extent of the lesion in the direction of the length of the brain stem was very slight. The posterior commissure was not divided.

The section (fig. 1) through the anterior thalamic region shows no sign of lesion or of degeneration except in

the internal capsule on the lateral side, due to accidental lesion of the hemisphere.

A section just below the thalamus (fig. 2), which reveals the fasciculus retroflexus in the greater part of its course, shows degeneration in the internal capsule of the lateral side, and also some degenerated fibres in the subthalamic white matter on the contralateral side running outwards horizontally in the position of the ansa lenticularis.

Sections passing through the posterior commissure and through the commissure habenulæ show no definite lesion, but the red nucleus on the contralateral side appears to be slightly damaged, and a few very fine fibres run from it in a dorso-lateral direction and quickly disappear.

In the posterior commissure a very few fibres are seen to be degenerated, some of them running out laterally into the white matter of the anterior corpus quadrigeminum on either side, others curving ventralwards in the direction of the median line and the red nucleus.

The degeneration in the pes pedunculi of the lateral side is still seen.

Degeneration is seen at the level of the superior colliculus in both tegmental decussations and in the oculo-motor nerve roots. In this region, too, there are a few degenerated fibres passing across the median line dorsal to the aqueduct.

Figure 3 represents a section through a lower part of the quadrigeminal region and through the decussation of the brachia conjunctiva. Degenerated fibres are seen in the descending root of the fifth nerve on the lateral side, in both dorsal longitudinal bundles, in both ventral longitudinal bundles and in a bundle of fibres henceforward to be called "Monakow's bundle," which is spreading out laterally on the dorsal surface of the fillet on either side. Comparing the two Monakow's bundles, one finds rather more degenerated fibres on the lateral side than on the contralateral side, due, probably, to the greater damage to the contralateral red nucleus.

At the decussation of the fourth nerve (fig. 4), Mona-

kow's bundle is seen to have taken up its position in the bend of the lateral fillet and to lie just ventral to the lower end of the brachium conjunctivum.

This position is maintained in the upper part of the pons (fig. 5). A section taken at the level of the trigeminal nerve figures the degenerated descending root of the fifth, leaving its central position to reach the surface, passing through the bend of the fillet and leaving Monakow's bundle in the ventral angle which it forms with that structure (fig. 6). The dorsal and ventral longitudinal bundles are still quite distinct and the degenerated fibres in the pyramid of the lateral side are plentiful.

In the lower section (fig. 7), which is rather oblique and cuts the eighth nerve on the lateral and the seventh nerve on the contralateral side, Monakow's bundle is seen in its relation to both, and to the superior olive and spinal root of the fifth nerve. It lies just medial to the outgoing facial root, just ventral to the trapezium and is bounded on its internal surface by the superior olive. Below the facial nerve the external boundary is formed by the spinal trigeminal root (fig. 7). In the same section the dorsal and ventral longitudinal bundles are seen to be more diffuse and less well-defined.

In fig. 8 Monakow's bundle is seen on either side occupying a part of the olivary-restiform angle and is indistinguishable in its position from Gowers' tract at that level.

At the decussation of the fillet (fig. 9) the dorsal and ventral longitudinal bundles form a rather more compact mass; Monakow's bundle maintains its relation ventral to the spinal root of the fifth nerve.

The course taken by the dorsal and ventral longitudinal bundles in reaching the anterior columns of the cord is well seen in fig. 10 where some pyramidal decussation is taking place. In the same figure the relation of Monakow's bundle to the direct cerebellar tract is represented.

The result of the pyramidal decussation is to force Monakow's bundle further anteriorly and to destroy its immediate relationship with the spinal trigeminal root

(fig. 11). All the degenerated fibres in the anterior columns now lie close alongside the median fissure.

Figures 12—14 represent sections of the cord taken in the cervical, mid-dorsal and lumbar regions respectively, and serve to show the relation of Monakow's bundle to the crossed pyramidal tract at the various levels of the spinal cord. It will be seen at once that it is only in the cervical region that the relative positions of these two tracts are at all easily distinguished owing to the characteristic shape of Monakow's bundle in this part. It seems to arise out of the middle of the crossed pyramid and to spread forwards in a sort of wedge, the apex of which reaches the surface of the cord in the anterior root zone region.

Monakow's bundle does not maintain this shape in the dorsal, lumbar and sacral regions of the cord, but is more incorporated with the crossed pyramid, appearing only as an anterior bulging of that tract.

In the sacral region (fig. 15) the number of fibres in the postero-lateral column of either side seems to be about equal, and these lie very near to the posterior root zone, a result which is probably due to the disappearance of most of the pyramidal fibres and the displacements dorsalwards of the fibres of Monakow's bundle.

*Comments.*—The degeneration in this experiment demonstrates the crossing of the fibres of Monakow's bundle and of the ventral longitudinal bundle in the tegmental decussations.

The greater degeneration in the Monakow's bundle on the side crossed to the lesion of the red nucleus suggests that these tracts are entirely crossed. The relation of these bundles to the radix descendens trigemini is well shown.

The fibres from the region of the dorsal commissure to the ventral longitudinal bundle of the same side again support Held's argument of uncrossed colliculo-spinal fibres.

*Experiment* 4.—Rhoesus monkey. Lesion in a sagittal direction to the right of the middle line extending from the soft commissure to the upper limit of the inferior colliculus.

The dorsal and habenular commissures were divided and the fasciculus retroflexus of the right side was involved.

Descending degeneration in the fillet as far as the medulla on both sides, in both descending trigeminal roots, in both dorsal longitudinal bundles and both ventral longitudinal bundles. (Plate XIII.—XIV.)

The lesion was produced in an attempt to divide the posterior commissure. The knife had entered obliquely at the middle of the soft commissure to the right of the middle line, and a linear lesion resulted which divided structures dorsal to the aqueduct on the right side and crossing the aqueduct from right to left had divided structures ventral to the aqueduct on the left side. The right fasc. retroflexus was injured, the dorsal and habenular commissures were completely severed to the right of the middle line. The line of the lesion entered the aqueduct and reached the third nuclei; from this point some damage, probably from hæmorrhage, extended ventrally and to the right into the nucleus lateralis superior and deep gray of the superior colliculus. The fourth nuclei were injured on both sides, but the lesion did not extend so far ventrally as the dorsal longitudinal bundles. Neither Meynert's nor Forel's crossways were damaged. The last trace of the lesion was seen in sections still showing the fountain crossway in the position of the right fourth nucleus.

Figure 1 is drawn from a section taken through the middle commissure showing the anterior end of the lesion. The only degenerated fibres at this level are those in the ansa lenticularis of the lateral and those in the internal capsule of the contralateral side.

The fasciculus retroflexus of the lateral side has been badly damaged by the lesion and many degenerated fibres are seen running towards its caudal extremity (fig. 2).

Figure 3 shows the destruction of the posterior and habenular commissures. From either side of the posterior commissure spring degenerated fibres, some of which run out laterally in the direction of the upper fillet, whilst others take a curved course ventralwards and either decussate in the mid-line or end in the neighbourhood of the red nucleus. Those fibres which run into the upper fillet are much more plentiful on the lateral than on the contralateral side.

An extension outwards of the lesion on the lateral side

of the Sylvian aqueduct in the superior quadrigeminal region increases the number of degenerated fibres coming from that side and entering into the formation of Meynert's decussation (fig. 4). At this level degeneration is seen in both dorsal longitudinal bundles, but more marked in that of the lateral side. The fibres of the fillet are seen sweeping round in a ventral direction; numerous on the lateral, scanty on the contralateral side. Both third nerves and the contralateral pyramid are degenerated.

Figure 5 represents a section taken through the decussation of the brachia conjunctiva. Here it will be seen that the fibres of Meynert's decussation have now turned caudalwards and lie just ventral to the dorsal longitudinal bundles. These are the fibres of the ventral longitudinal bundles and rapidly take a more ventral position, running, as they do so, amongst the decussating fibres of the superior cerebellar peduncles. At this level degeneration of both descending trigeminal roots is noticed and from each a few fibres appear to spring and run out in a ventro-lateral direction. The degenerated fillet fibres do not take identical positions on either side, those on the lateral side turning caudalwards earlier and at a greater distance from the mid-line than those on the contralateral side. The lowest end of the lesion is seen in the same figure in the shape of slight damage to the ventral wall of the aqueduct.

At the decussation of the fourth nerves (fig. 6) the ventral longitudinal bundles have taken up the position which they maintain to the lower end of the pons.

Figure 7 represents the degenerated descending trigeminal roots making their way to the surface to join the main nerve-trunk.

In the medulla (fig. 8) the ventral and dorsal longitudinal bundles have become more or less fused. The fillet fibres on either side have become scattered and no longer constitute a compact bundle; some are seen in the reticular formation and some hug the dorsal and lateral aspect of the inferior olives. On the contralateral side there are a few degenerate fibres belonging to the pyramidal system which lie lateral to the main pyramidal mass, and these fibres can

be traced into the cervical cord in an uncrossed path (see figs. 9 and 10).

At the level of the decussation of the fillets the fibres belonging to the longitudinal bundles sink further ventralwards and are forced into a more lateral position by the decussation. Tracing these fibres into the cervical cord (fig. 10), it will be noticed that on the contralateral side more fibres remain near the lip of the anterior median fissure; these may be supposed to belong to the ventral longitudinal bundle system, whilst the fibres which have sunk deeply along the margin, being more numerous on the lateral side, are probably continuous with the dorsal longitudinal bundles.

Fibres in both these positions can be traced in decreasing numbers down to the lumbo-sacral region of the cord.

Below the decussation of the pyramid a few degenerated fibres are to be found in the postero-lateral region of the contralateral side, and these undoubtedly are uncrossed fibres from the degenerate pyramid above.

In figs. 10 and 11, taken respectively from sections in the cervical and sacral parts of the cord, degenerated fibres belonging to a root system appear in the posterior columns. For some unknown reason, degeneration of one or more posterior roots at the lower extremity of the cord has taken place, and the fibres can be traced through their entire course upwards into the posterior column nucleus of the lateral side.

*Comments.*—The degeneration of the fillets seemed to correspond with the lateral expansion of the lesion in this animal as compared with the other experiments. As regards the ventral longitudinal bundles, the same remarks apply in this as in the other cases.

*Experiment* 5.—Cat. Lesion of right optic thalamus limited between soft commissure and dorsal commissure; not reaching wall of ventricle and not destroying corpus subthalamicum.

Degeneration behind lesion in post commissure, and in a bundle lying immediately ventro-lateral to the dorsal longitudinal bundle of side of lesion and extending into the medulla and spinal cord, in stratum opticum and in upper fillet. (Plate XV.)

The lesion was produced in an attempt to divide the frenulum habenulæ of the right side by puncture through the corpus callosum. There was a somewhat rounded hæmorrhage measuring 5 mm. transversely and 3 mm. vertically (the puncture mark in the surface of the thalamus was midway between the soft and dorsal commissures); it involved chiefly the anterior part of the red nucleus and region immediately external to this. From a slight injury to the left marginal convolution some fibres of the left pyramidal system were degenerate. In front of the lesions some degenerate fibres ran outwards, forwards and downwards, and ended in the right corpus Luysii, others running into the right ansa lenticularis; many ran outwards and into the right optic radiation. The optic tracts, Vicq D'Azyr's bundle and Meynert's bundle and commissure, with the ganglion habenulæ, were normal.

From the mesial aspect of the lesion a few fibres crossed the dorsal commissure and immediately disappeared in the neighbouring gray matter.

From the caudal limit of the lesion a copious stream of degenerated fibres ran back, and in sections still showing the dorsal commissure were seen to divide into three groups, "A" entering the stratum opticum of the superior colliculus, "B" entering the region of the fillet, "C" forming a compact bundle at some distance ventro-lateral to the Sylvian aqueduct.

Group "A," composed of very coarse fibres, gradually broke up and disappeared in the stratum opticum. Group "B," composed of numerous very fine fibres, lost many fibres in the region of the red nucleus and substantia nigra, and entered the right mesial fillet. Dropping ventrally in their course and gradually thinning out, these fibres were no longer traceable at the level of the exit of the trigeminus.

Group "C" formed a most conspicuous and compact bundle of large fibres which coursed caudalwards, maintaining a constant position ventro-lateral to the right dorsal longitudinal bundle. (There were no degenerate fibres in either d.l.b.) This tract was everywhere quite separate from the d.l.b. and from the ventral longitudinal bundle.

The fibres became much reduced in number but not in size below the level of sixth nucleus. In the lower medulla the fibres lay on either side of the middle line, having a position between those of the d.l.b. and the v.l.b. and lateral to both. They entered the anterior column of the cord with these tracts, reduced in number below the decussation of the pyramid to about six coarse fibres, some of which were traced to the lumbar region of the cord. With the exception of the slight degeneration of the left pyramid, which was traceable to the sacral region, no other degeneration was found in the nervous system.

*Comments.*—The degeneration of the fillet fibres very intense at first and rapidly diminishing caudally, none being traceable into the medulla, was striking. They apparently ended in the nuclei pontis. We have not been able to find any mention of such fibres in the literature.

The fibres of group "C" were certainly thalamic in origin and held a straight course. They were certainly not fibres of the Haubenbahn. Nor from their course and termination did they appear to belong to the group of the mesial fillet.

In sections of the pons they at first sight appeared to be part of the ventral longitudinal bundle. They did not arise in the gray matter of the superior colliculus and do not therefore correspond with Held's uncrossed tecto-spinal fibres. The tract was apparently an uncrossed descending thalamic tract, to the ventral columns of the cord.

### Pathological Degenerations.

*Case* 1.—Tumour involving almost the whole of the dorsal two-thirds of the mesencephalon in the region of the superior colliculus involving the pulvinar thalami and the left capsule.

Degeneration below the lesion in the left pyramid; both central tegmental tracts, both Monakow's bundles, both brachia conjunctiva R. > L.; both descending roots of the fifth nerve and in both mesial fillets L. > R. (Plate XVI.—XVII.)

*Clinical abstract.*—B.M., aged 15 years, admitted into the National Hospital on July 6, 1900, under the care of Sir William Gowers.

Total duration of symptoms one year.

Chief symptoms: Right hemiparesis, total hemianæsthesia to all forms on right side; right knee-jerk absent, complete incontinence of sphincters, ocular palsies. Blindness from consecutive optic atrophy.

*Anatomy.*—The tumour was strictly limited and hard in consistence with many recent hæmorrhages in its substance. It was a granuloma perhaps of tuberculous nature. It involved the left thalamus and left internal capsule, slightly the right thalamus. Its upper limit in the thalamus was the soft commissure. A tongue of growth extended into the left tegmental region as low as the lower part of the inferior colliculus. A section at the level of the anterior part of the superior colliculus showed that the growth involved the whole mesencephalon at that level, except the right pyramid and substantia nigra and a portion of the ventro-lateral region on the left side and the commencement of the crossing fibres of the pons. In the first section below the main lesion clear of the "traumatic degeneration" the left pyramid was intensely degenerated and the degenerate fibres showed signs of having been more recently affected than those of the other tracts about to be described. The pyramidal degeneration as regards its course, decussation and termination showed no peculiarity. Both superior cerebellar peduncles showed a great many degenerate fibres R. > L. which were traced to the interior of the dentate nucleus and to the cortex of the lateral cerebellar lobes. Both fourth nerves and both descending roots of the fifth nerve were degenerate and showed no peculiarity worthy of special mention. The dorsal longitudinal bundles and ventral longitudinal bundles were much degenerated and of the former chiefly its dorsal and mesial fibres. The v.l.b.'s were conspicuously distinct with their passage into the anterior columns of the cord where they mixed with the d.l.b.'s and anterior pyramidal degeneration. They were situated some little distance lateral to the raphe and sank farther and farther from the d.l.b.'s in their course caudalwards. The fibres were easily distinguishable from the fibres of the degenerate fillets in the inter-olivary layer by their being much larger. Both

Monakow's bundles were degenerated and their course so closely resembled that already described in the cat and monkey that it is sufficient here to describe certain important points only. The decussation of these fibres in Forel's decussation was plainly seen. From the exit of the facial nerve to the second cervical segment these tracts kept much more closely to the ventro-mesial aspect of the spinal fifth and did not reach the surface in the olivo-restiform angle nor spread downwards to the inferior olive. In the region of the decussation of the pyramids they were situated far more dorsally and deeper than in the cat and monkey and were ventral to the substantia gelatinosa. When the pyramid had crossed the tracts had the form of an elongated equilateral triangle with narrow base on the surface of the cord and apex touching the outer surface of the lateral pyramidal tract. Below this the tracts became fusiform and the external point of the spindle turned forwards to the ventral root region. The fibres were not distinguished from the crossed and contra-lateral pyramidal degeneration below the fifth cervical segment.

The fibres were large but few in number. It is possible that on account of the age of the degeneration much of the Marchi reaction had been lost. (Indeed specimens of this case mounted in the ordinary way showed little or no trace of any degeneration except the pyramidal an hour after they were mounted, but only a dark cloud. This was obviated by rapid clearing, mounting uncovered on a glass plate in hot thick balsam and drying rapidly in hot air. Hamilton's modification of Heller's method for fixing old degeneration, combined with rapid desiccation of the balsam was also used.)

The left mesial fillet showed many degenerate fibres, a few only being present in the right mesial fillet. The former descended into the left half of the interolivary layer, where many entered the stalk of the left inf. olive, and some crossing the raphe entered the right inf. olive. Many of these fibres passed downwards and disappeared in the region of the pyramidal decussation. Some of them crossed in the fillet decussation, and were traceable into the region of the

dorsal column nuclei. None were traced into either lateral column of the cord. The degenerated fibres in the right fillet had a similar course. Next to that of the left pyramid the most conspicuous degeneration was that of the "Centrale Haubenbahn" on either side. At the level of the posterior part of the decussating brachii two large fusiform areas of degeneration were visible, plainly showing to the naked eye in the degenerate decussation the long axis, vertical and reaching on either side from the d.l.b. almost to the mesial fillet. Traced upwards into the region of the lesion the right tract was not obscured by the lesion for some distance and lay immediately mesial to the hinder end of the red nucleus and above a conspicuous degenerated Monakow's bundle.

Traced downwards the tracts kept close and mesial to the uprising brachia, and at the level of the fourth decussation formed the "star" to the crescentic outline of each brachium; the central position of the tracts in each lateral half of the dorsal brain stem which led Bechterew to name the tract "Centrale Haubenbahn" was conspicuous. Immediately below this level each tract sank sharply down and ran as a large round bundle close dorsal to the middle of the mesial fillet, and where the latter structure began to break up in the interolivary layer it crossed ventro-laterally and lay first close dorsal and then external to the inferior olive. The fibres could be traced round the sheath of the olive and between this and the pyramid, much reduced in numbers, and appeared to end in the olive.

*Comments.*—This case is interesting from the association of complete hemianæsthesia to all forms with a lesion completely destroying one half of the tegmental region. The important points in connection with the degenerations below the lesion are:—(1) The presence of Monakow's bundles, their decussation in Forel's crossway, and their course and terminations being identical with the same tracts described in the lower animals; (2) The presence of the central tegmental tract in man and its termination in great part in the inferior olive; (3) The separation of the ventral longitudinal bundles as distinct and well marked tracts; (4) The des-

cending degeneration in the mesial fillets and in the brachia conjunctiva.

*Case* 2.—Abscess of the tegmental region, anterior limit at the foramen of Monro. Posteriorly reaching into the superior medullary velum as far as the commencement of the vermis. Involving chiefly the left corpus subthalamicum and left quadrigeminal region. At the level of the upper part of the pons the whole of the mesencephalon dorsal of the mesial fillet was destroyed.

Degeneration in a tract on either side, running from the superior medullary velum to Deiters's nucleus.

Degeneration of both dorsal longitudinal bundles, both ventral longitudinal bundles, both central tegmental tracts, both brachia conjunctiva, both descending trigeminal roots, both Monakow's bundles, and in both mesial fillets, and (slight) in both pyramids.

Marked atrophy of the left inferior olive. (Plate XVIII.—XIX.)

Below the thalamic region the abscess cavity was confined entirely to the tegmental region, and posteriorly spread into the superior medullary velum, pressing the superior cerebellar peduncle ventralwards. Its posterior limit was on the left side in the roof of the fourth ventricle.

The pyramidal degeneration was slight and was more marked upon the left side. The central tegmental tracts were first seen ventral to the lesion and mesial to each distorted superior brachium. They descended to the dorsal aspect of each mesial fillet, and in this position each had the form of a large round bundle. They then dropped ventralwards at the commencement of the interolivary layer to course round the external and then the ventral aspect of the inferior olive, and were lost in the interolivary layer immediately dorsal to the pyramids. The fibres of these tracts were very fine. No connection of these tracts with the triangular field could be made out.

The degenerated fibres in the mesial fillet descended, after giving off many fibres to the region of the facial nucleus, into the interolivary layer, and many fibres entered the inferior olive; other fibres were traced across the fillet decussation to the posterior column nuclei.

The course of the degenerated fibres of Monakow's bundle was typical. In sections taken rather obliquely

through the pons, the dorsal limit of the section being some distance in front of the ventral limit, the central tegmental tract and Monakow's bundle were seen on each side, their fibres running in the plane of the section parallel to one another as they descended to the olivo-restiform angle, the two tracts enclosing the superior olive and nucleus facialis. The contrast of the coarse fibres of Monakow's bundle and the fine fibres of the central tegmental tracts was very striking.

In the fasciculus proprius lateralis medullæ these two tracts occupied the ventral limit and the dorsal limit of this region respectively, the central tegmental tract lying in contact with the olive, and Monakow's bundle being situated immediately ventral to the spinal root of the fifth.

In the cord Monakow's bundle took the form of a fusiform area, stretching in a dorso-mesial direction deeply into the lateral column from the lateral limit of the anterior roots. Below the upper dorsal region the fibres were blended with the few degenerate fibres of the lateral pyramidal tract.

The dorsal and ventral longitudinal bundles were distinct as far as the fillet decussation, and were followed to the sacral region lying on either side of the ventral fissure.

Traceable directly out of the posterior part of the lesion in the superior medullary velum, a well-marked band of fibres ran ventrally and caudally along the mesial aspect of each superior cerebellar peduncle, lying between this and the ependyma. These tracts were traceable directly into Deiters's nucleus where they broke up and ended. None of these fibres could be traced into the region of the nucleus of the vagus.

*Comments.*—This case serves to demonstrate Monakow's bundle and the central tegmental tracts as tracts which degenerate downwards in man, in lesions of the mesencephalon. The localised lesion of the valve of Vieussens, with a tract of degeneration on either side running thence to Deiters's nucleus, is of interest. These tracts are very conspicuous in transverse sections of the pons of infants stained by Pal's method. They have been studied developmentally

by Kolliker and by Edinger, using degeneration methods, in both man and the higher vertebrates. They are described as having their origin in the nucleus fastigii and possibly also in the nucleus emboliformus and nucleus globosus, and as running on one hand to the nucleus of Deiters, on the other hand to the nucleus vagi. Kolliker's investigations by Golgi's method suggest, however, that some of the fibres of these tracts have their origin in the nucleus vagi and in Deiters's nucleus and ascend to the roof nuclei of the cerebellum.

*Case* 3.—Tumour of the pons extending from the region of the inferior colliculi to the junction of the pons and medulla, more extensive upon the left side.

Descending degenerations in both pyramids L. > R.; in the left mesial fillet and central tegmental tract; left fasciculus proprius lateralis of the medulla; in both dorsal and the right ventral longitudinal bundle; left spinal trigeminal root. Atrophy of the left inferior olive. (Plate XX.)

*Clinical abstract.*—R. D., aged 42 years, admitted into the National Hospital, under the care of Dr. Ormerod, on March 19th, 1901. Duration of symptoms ten months. Course of symptoms. Numbness of right hand and leg, right hemiplegia; numbness of left hand, paresis of left hand; complete bone deafness of left ear; left fifth, sixth and seventh nerve palsies; dysphagia and dysarthria. (The left leg had been amputated.)

The tumour was a glioma which had undergone degeneration and it contained many hæmorrhages. It implicated almost the whole of the left half of the pons from the inferior colliculus to the upper end of the inferior olive, and it extended across the middle line in the middle pontine region.

The degeneration of the left pyramid presented no peculiarity. The degeneration in the right pyramid was entirely confined to the outer third of the pyramid in the medulla; these degenerate fibres crossed entirely at the decussation and occupied a position in the lateral column close to the dorsal horn. The spinal fifth was traced to the upper part of the third cervical segment. The central

tegmental tract was first recognisable lying above the mesial fillet and had a characteristic course round the olive. It was traced between the pyramid and olive, losing many fibres on the latter, and some of its fibres seemed to end by entering the hilum of the inferior olive, and possibly some crossed the middle line to enter the contralateral inferior olive.

The degenerated fibres of the fillet in part entered the inferior olive, but most of them crossed in the fillet decussation and ended in the region of the posterior column nuclei. The degeneration of the right ventral longitudinal bundle was distinguishable from that of the dorsal longitudinal bundle as far as the decussation of the pyramids and the degeneration of these tracts was traced to the lowest sacral region lying on either side of the ventral fissure. The degeneration of the fasciculus proprius lateralis medulla occupied the dorsal part of the olivo-restiform angle, ventral to the degenerate spinal root of the fifth. In the spinal cord this degeneration was arranged as a band of scattered fibres stretching from the anterior column degeneration to the outer limit of the anterior roots, and continuous with this a copious wedge-shaped area of degeneration with base at the surface of the cord dorsal to the anterior root, and apex stretching into the crossed pyramidal tract. This degeneration in the antero-lateral region was traced in this position to the lumbar region.

*Comments.*—The degeneration in the fasciculus proprius lateralis medullæ was probably made up of Monakow's bundle, the lateral ponto-spinal tracts, and the vestibulo-spinal tract. The distribution of these fibres on reaching the spinal cord was that of the vestibulo-spinal tract (Russell) and Monakow's bundle. The termination of the central tegmental in the triangular area of Helweg was most certainly not present.

*Case* 4.—Tumour of the pons and upper medulla with practically complete destruction of the lower pons; the left pyramid and the left inferior olive being the only recognisable structures in sections stained by Heller's method.

Degeneration in both ventral columns, both antero-lateral columns, both lateral columns; the direct cerebellar tract and Gowers' tract alone escaping. (Plate XXI.)

*Clinical abstract.*—M. S., aged 5½ years, admitted into the National Hospital, under Dr. Ferrier, on September 7, 1900. Duration of symptoms nineteen months. Course of symptoms: Diplopia, right hemiplegia and hemiataxy; paralysis of the left fifth nerve; incontinence of urine; optic atrophy; complete flaccid paraplegia; loss of deep reflexes.

The growth was a hard glio-sarcoma. It extended from the level of the exit of the fifth nerve to the middle of the inferior olives. Its sagittal extent was much greater upon the left side. At the level of the junction of the pons and medulla it involved almost the whole transverse section of the brain stem.

In the cervical region of the spinal cord almost the whole of the anterior and lateral columns were degenerate, with the exception of the regions occupied by the direct cerebellar and Gowers' tracts, some fibres of the anterior column around the median fissure, and some fibres round the gray matter of the ventral horns. The regions of the pyramidal tracts and antero-lateral descending tracts showed much old degeneration by the Marchi method, and the degeneration was still more striking in sections stained by Weigert's method and van Gieson's method. There was some degeneration in all the anterior roots of the cervical region.

In the other regions of the spinal cord the degeneration occupied the same positions, but became less extensive in lower regions of the cord; it was traced to the lowest sacral region. In the sacral and lumbar regions there was marked degeneration of the posterior roots (not figured).

*Comments.*—The maintenance of life, even of a merely vegetative nature, was remarkable, considering the extensive nature of the lesion, which apparently amounted to a total transection of the brain stem at the junction of pons and medulla. The degeneration was very great in the ventral and lateral columns, and practically only in the ascending tracts and in the region of the short internuncial fibres round the gray matter, were normal myelin sheaths to be seen, and consecutive sclerosis had altered the shape of the spinal cord; the ventral regions being much thinned. The degeneration of the anterior roots in the cervical region

was interesting. It does not seem probable that it was of the nature of a degeneration from disuse, for we have failed to find any such degeneration below the lesion in cases of total transverse lesions of the spinal cord, even when life has been prolonged for many months after such injury. It is possible that this degeneration of the ventral roots is of the same nature as the degeneration of the posterior roots, which frequently occurs in connection with intracranial tumours. Both the intramedullary and extramedullary roots were degenerated. There was in this case much recent degeneration of the posterior roots, and this was most marked in the sacral region. This has not been inserted in the diagram.

*Case* 5.—Tumour of left centrum ovale, involving the left internal capsule. A localised patch of recent softening was present in the superior collicular region, involving the nucleus lateralis superior, the upper part of the substantia nigra, the upper fillet, and, slightly, the outer side of the red nucleus on the left side. A small hæmorrhage was present in the posterior inferior part of the left inferior colliculus.

Degeneration below the lesions in the left pyramidal tract, accessory fillet, and mesial fillet.

From the lesion in the inferior colliculus a large fibred tract descended, having a dorso-lateral situation in the pons and medulla, and in part, joining the pyramid at the decussation, appeared to run as a ventro-lateral tract in the cord.

G. B., aged 54 years, was admitted into the National Hospital under the care of Sir William Gowers. Duration of symptoms eight weeks. No symptoms present till eight weeks before death, when a sudden attack of right hemiplegia and aphasia occurred. A second attack ten days later. No optic neuritis, headache, nor vomiting. No hemianæsthesia. Deep reflex increased. (Plate XXII.—XXIII.)

The tumour was a large soft glioma with much softening and hæmorrhage in its substance. It involved the whole thickness of the central part of the internal capsule, but the anterior part of the anterior limb and the posterior part of the posterior limb escaped. A recent softening was present in the left mid-brain at the level of the outgoing third nerve, involving the region of the upper fillet, the outer part of the

nucleus lateralis superior and nucleus ruber, and the upper part of the substantia nigra. A recent hæmorrhage was present, involving the left lateral fillet in the angle between the left superior brachium and left mesial fillet.

The degeneration of the left pyramidal fibres occupied the middle two-thirds of the crus. At the decussation of the pyramid well-marked ventral and lateral homolateral bundles were present, and a ventral crossed bundle was present.

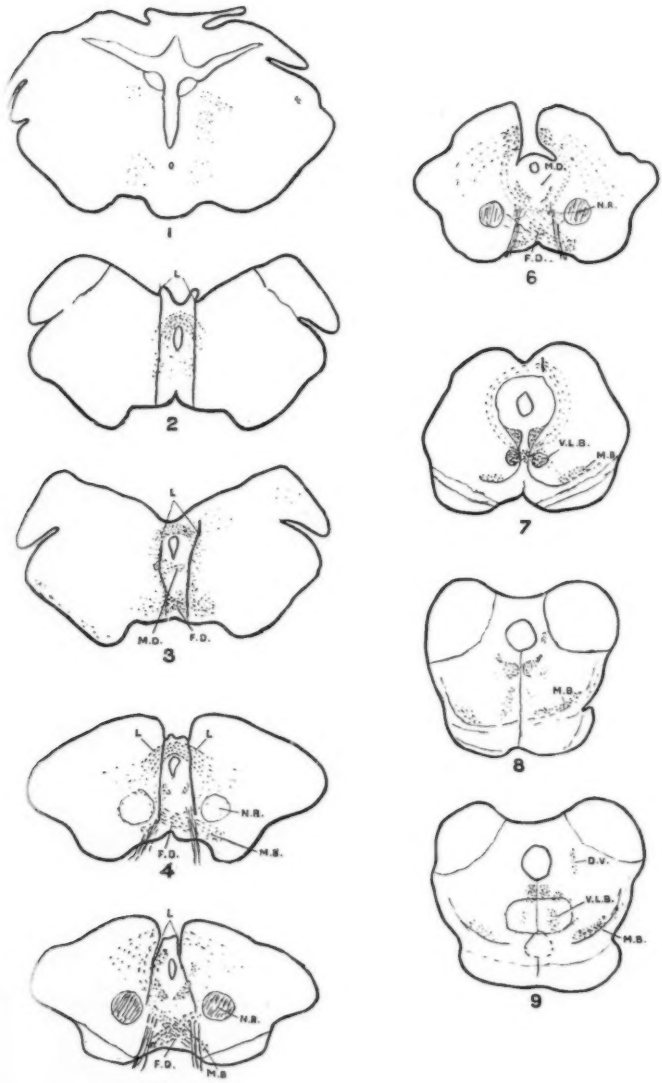
Conspicuous in sections of the upper part of the mid-brain was a large bundle of fibres lying in the concavity of the left crus, between this and the substantia nigra (accessory fillet). This bundle rose above the most lateral fibres of the crus in its descent and on entering the pons left relation with the pyramidal fibres and entered the mesial fillet, some of the fibres lying in layers between this structure and the pyramidal bundles. In the pons many of these fibres were seen coursing ventrally, apparently to enter the pyramidal bundles, others ended in the nuclei faciales and hypoglossi of the same and of the opposite side, others descended into the interolivary layer and apparently entered the left pyramid.

Distinguishable from the accessory fillet fibres were other degenerate fibres in the mesial fillet traceable from the lesion in the quadrigeminal region. These were followed into the interolivary layer of the left side.

From the lesion in the region of the left lateral fillet a well-marked band of large fibres was traced downwards, having a straight course through the lateral region of the pons in the upper part of its course lateral to the superior brachium below lateral to the restiform body. It reached the surface of the medulla at the level of the exit of the tenth nerve where it lay on the dorso-lateral surface of the restiform body as a very compact triangular tract with the base on the surface. In the lower medulla these fibres ran sharply downwards over the surface of the lateral column to the antero-lateral region.

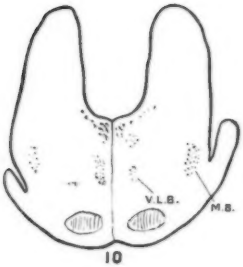
*Comments.*—This case exemplifies very well the four tracts into which the pyramid splits at the decussation

PLATE I.




Cat. Division of dorsal commissure, Meynert's decussation and Forel's decussation in part. Degeneration below the lesion in both Monakow's bundles, R. > L.; both dorsal longitudinal bundles, and in the right ventral longitudinal bundle. *Projection drawings.*

PLATE II.



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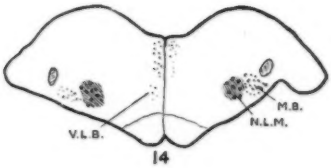

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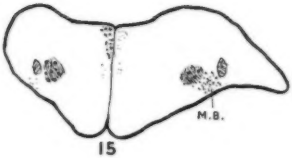

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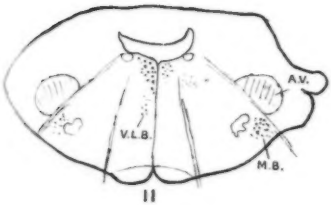

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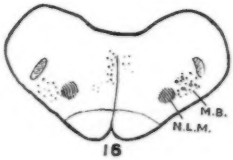

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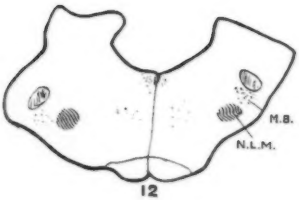

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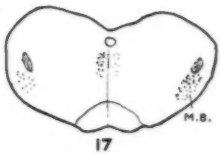

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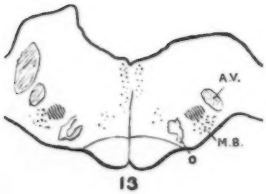

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PLATE III.

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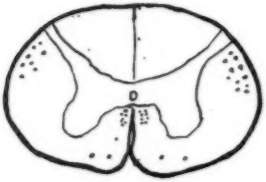

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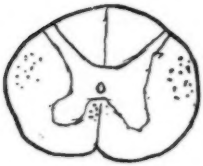

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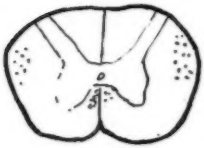

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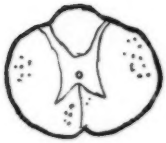

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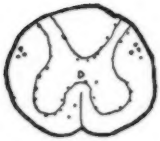

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PLATE IV.

FIG. 1.

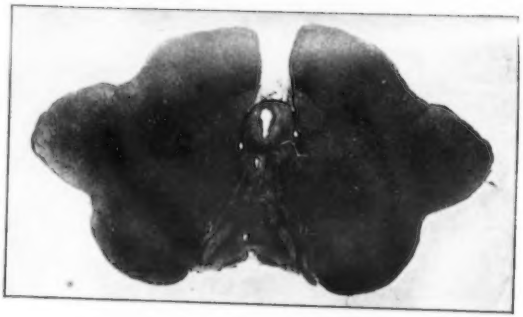


FIG. 2.

FIG. 3.

FIG. 4.

*The same. Photographic reproductions.*

FIG. 5.

FIG. 6.

FIG. 7.

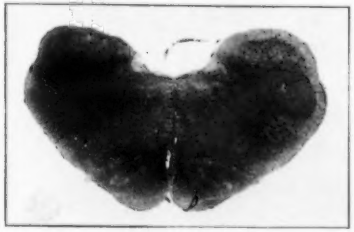


FIG. 8.

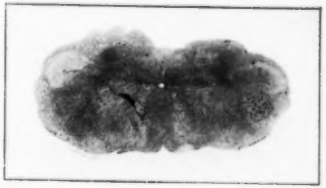
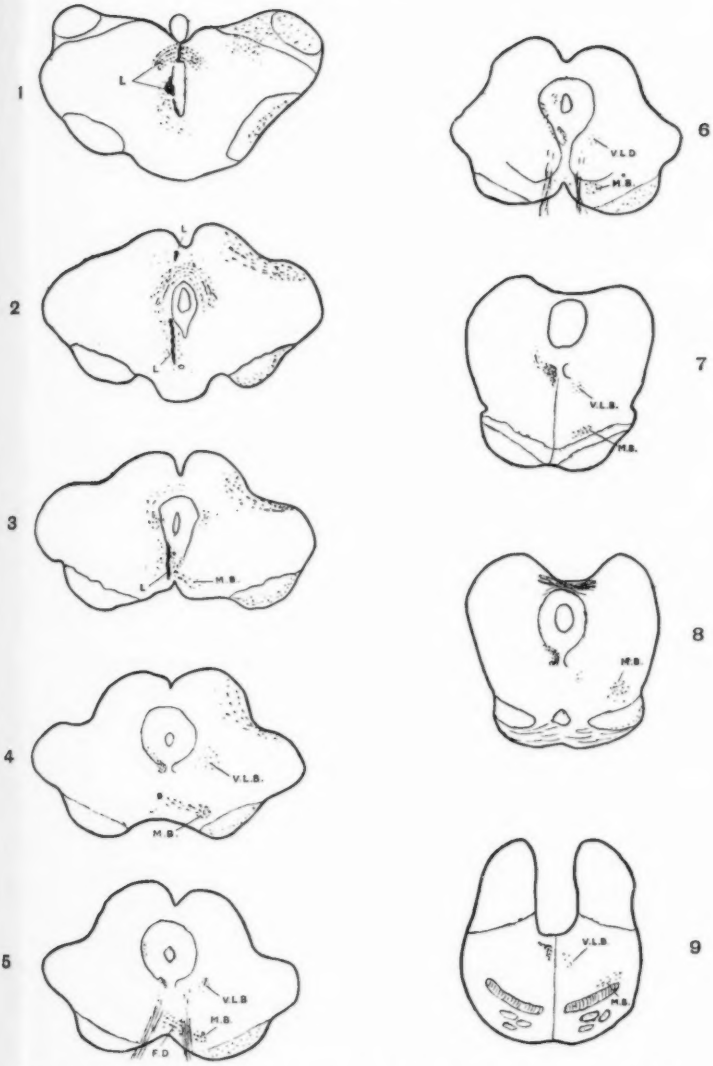


FIG. 9.

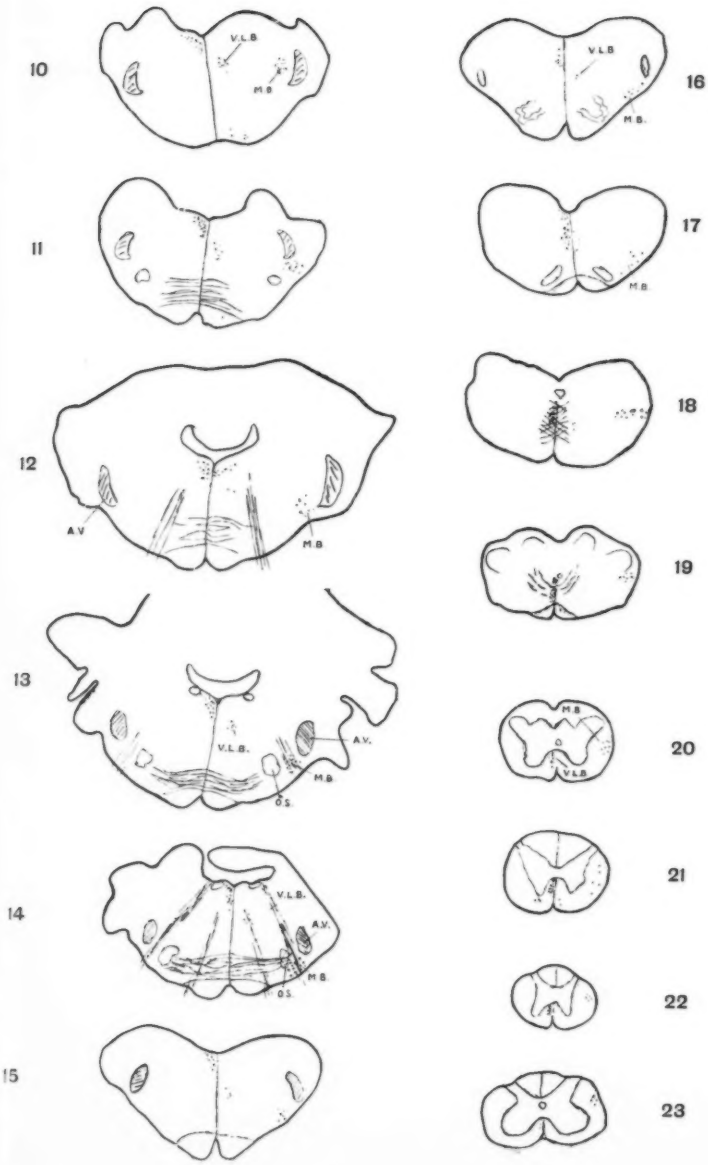
*The same. Photographic reproductions.*

## PLATE VI.




Cat. Sagittal linear lesion of mesencephalon to the right of the middle line. Degeneration below the lesion in right dorsal longitudinal bundle, left ventral longitudinal bundle and in the left Monakow's bundle. *Projection drawings.*

# PLATE VII.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V.L.B.
M.B.
11
12
A.V.
M.B.
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V.L.B.
A.V.
M.B.
O.S.
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V.L.B.
A.V.
M.B.
O.S.
15
16
V.L.B.
M.B.
17
M.B.
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M.B.
V.L.B.
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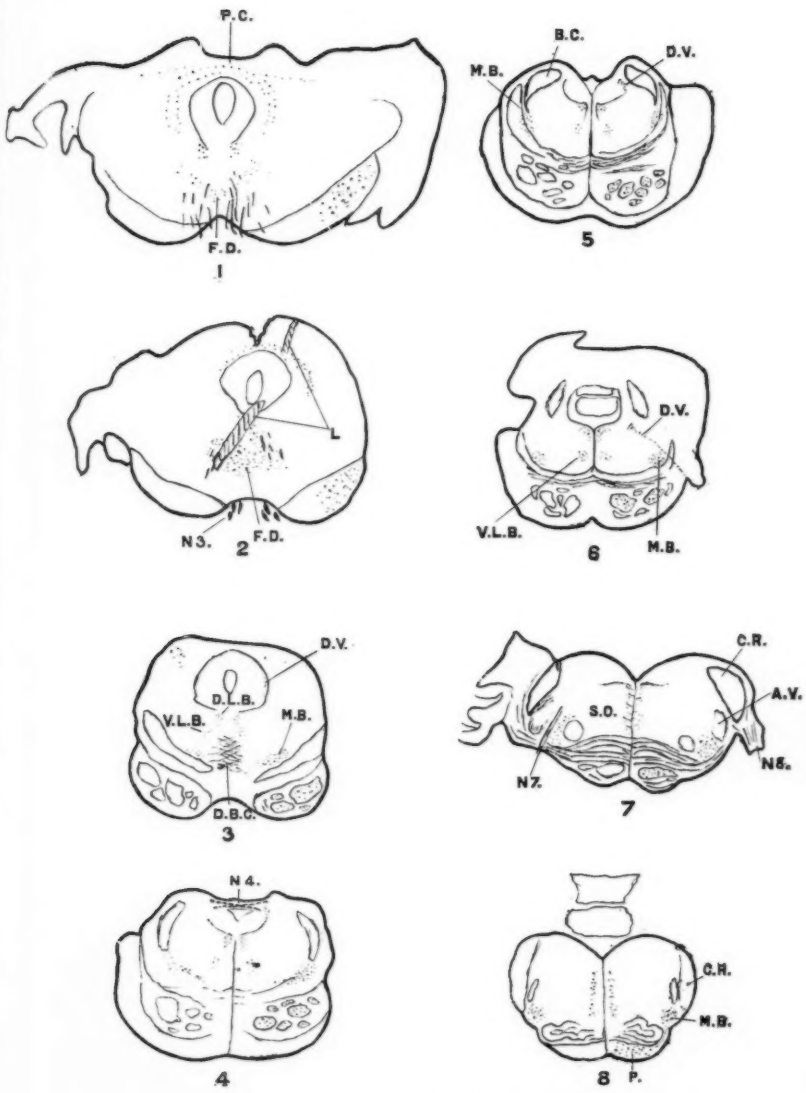
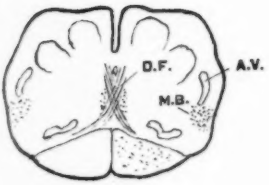
## PLATE VIII.




Monkey. Lesion in R. superior colliculus running obliquely into region of left red nucleus. Degeneration in both Monakow's bundles, in both dorsal and ventral longitudinal bundles, in the right descending root of 5th nerve, and in one pyramid. *Projection drawings.*

PLATE IX.

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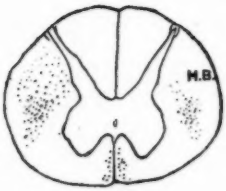


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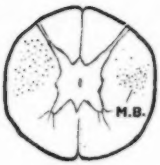


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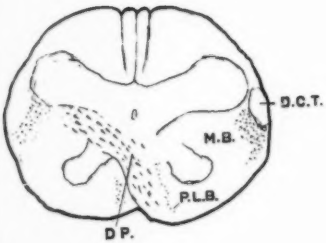


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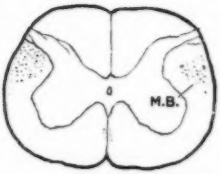


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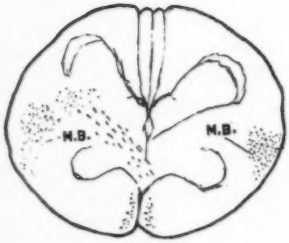


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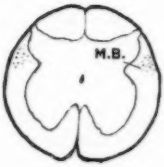


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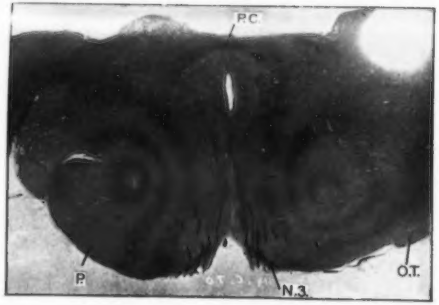
Fig. 1.



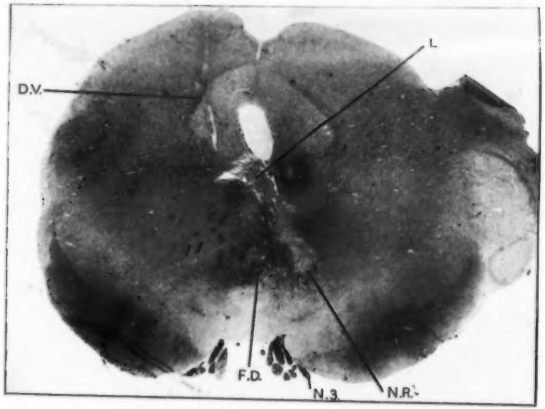
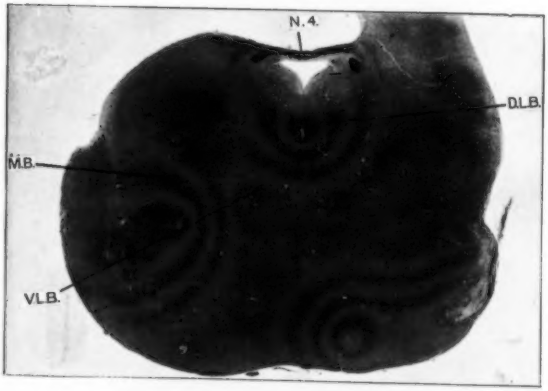




Fig. 2.

Fig. 3.



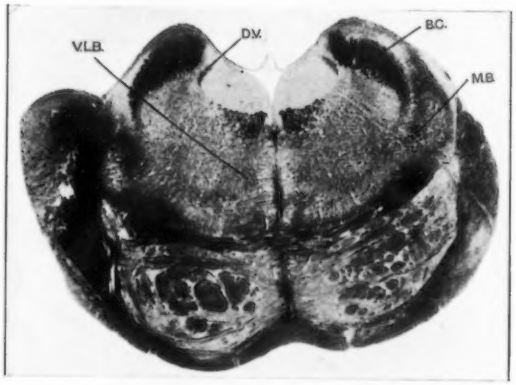




Fig. 4.

*The same. Photographic reproductions.*

PLATE XI.

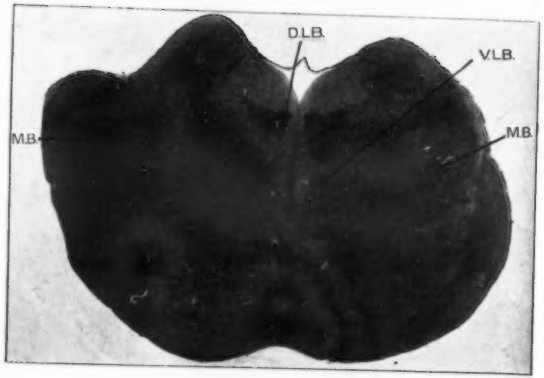



FIG. 5.

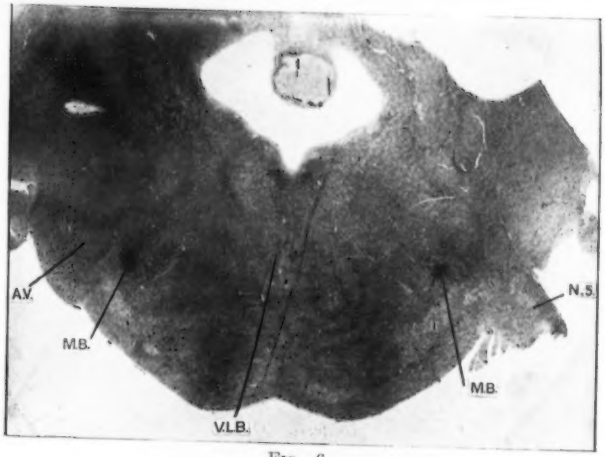



FIG. 6.

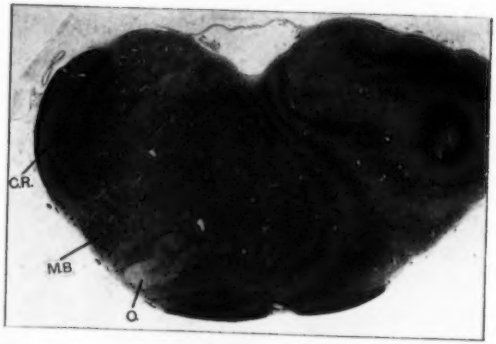



FIG. 7.

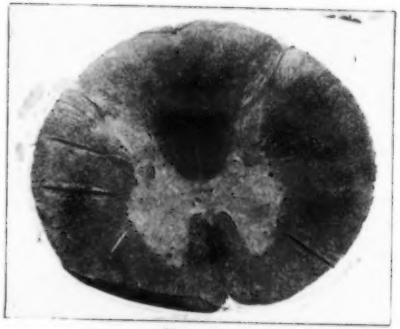


FIG. 8.

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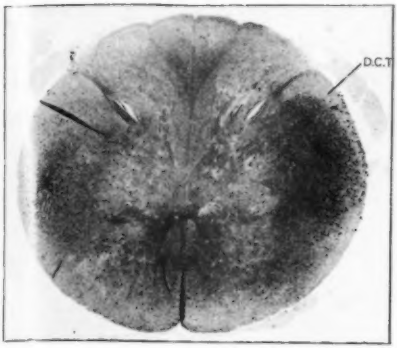



FIG. 9.

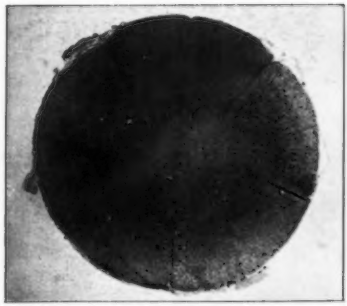


FIG. 10.

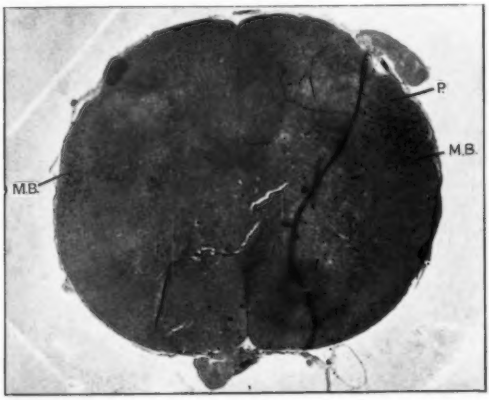



FIG. 11.

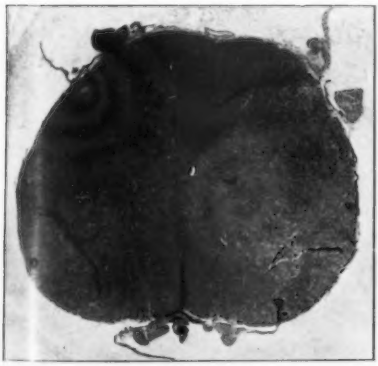


FIG. 12.

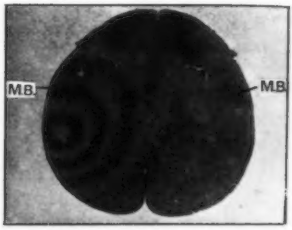
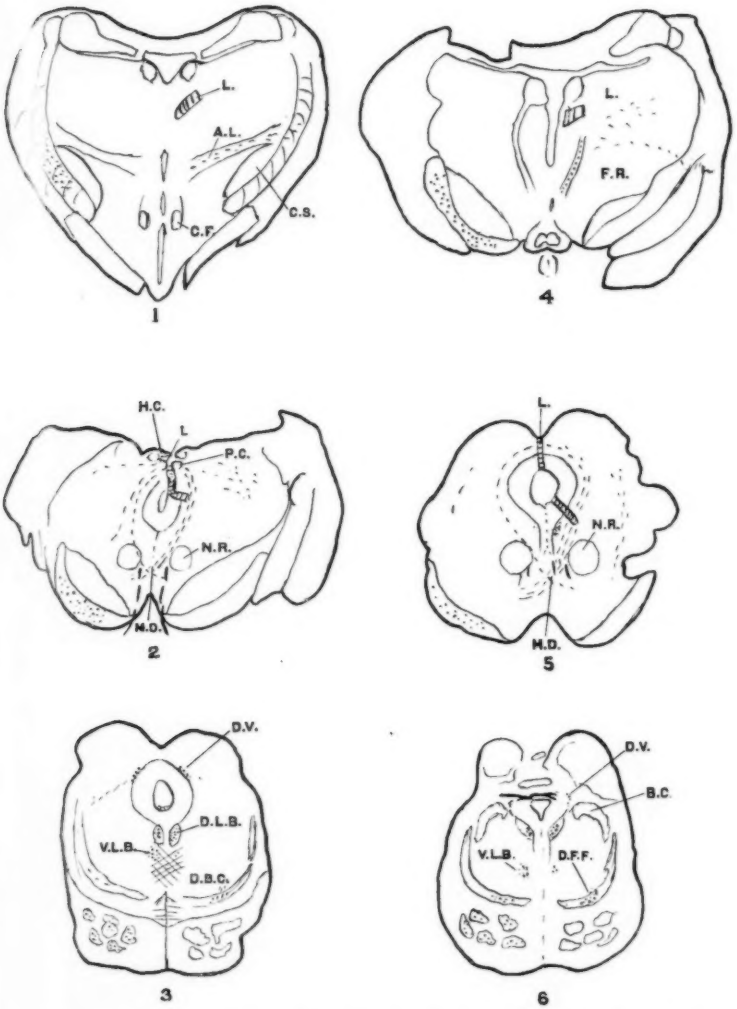



FIG. 13.

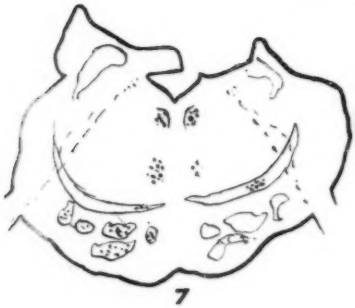
*The same. Photographic reproductions.*

PLATE XIII.




Monkey. Lesion extending from soft commissure backwards to the inferior colliculus, dividing the posterior commissure and destroying much of the gray matter around the Sylvian aqueduct. Degeneration in both dorsal and ventral longitudinal bundles, in both descending roots of 5th nerve, in descending fillet fibres on both sides and in one pyramid. *Projection drawings.*

PLATE XIV.



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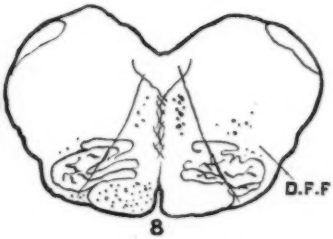


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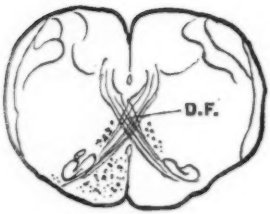


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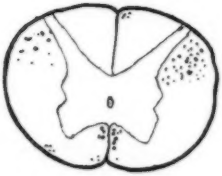

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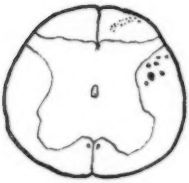

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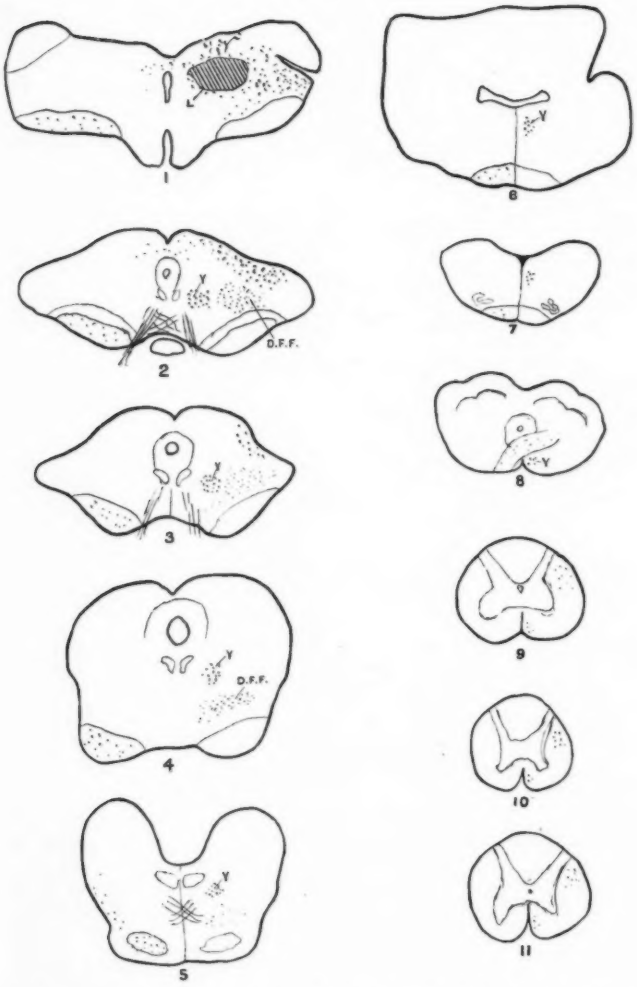
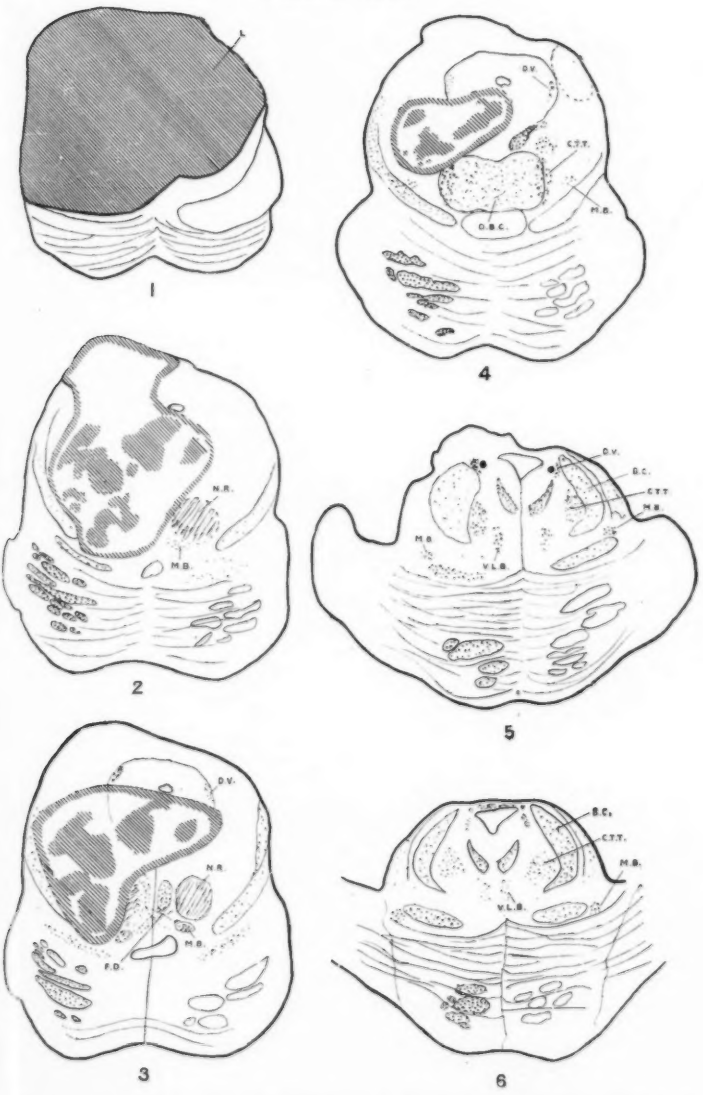
PLATE XV.



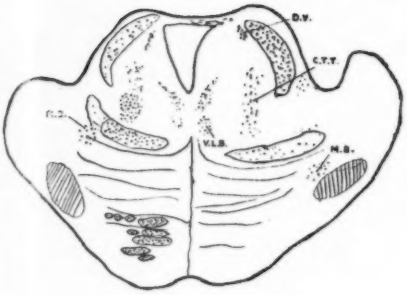

Cat. Lesion of right optic thalamus. Degeneration behind lesion in post commissure, and in a bundle lying immediately ventro-lateral to the dorsal longitudinal bundle of side of lesion and extending into the medulla and spinal cord, in stratum opticum and in upper fillet. *Projection drawings.*

## PLATE XVI.




Tumour of mesencephalon. Descending degeneration in the left pyramid, both central tegmental tracts, both Monakow's bundles, both brachia conjunctiva, both descending trigeminal roots and in both mesial fillets. *Projection drawings.*

# PLATE XVII.

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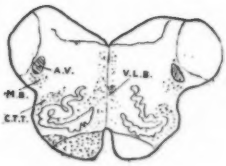


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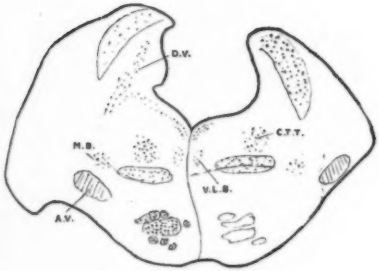


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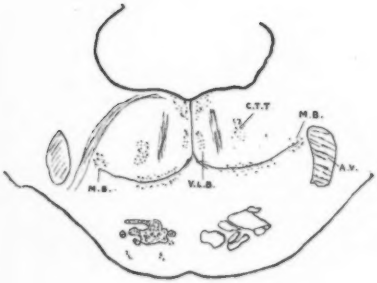


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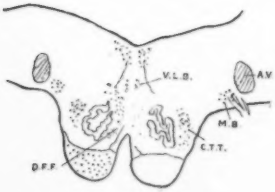


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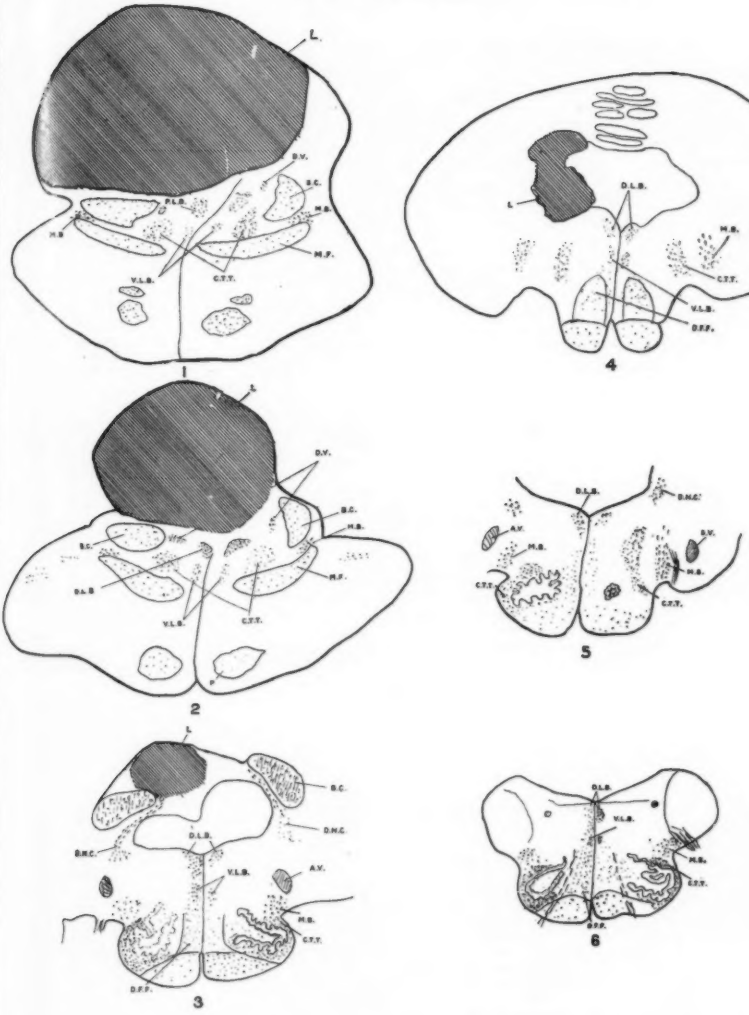
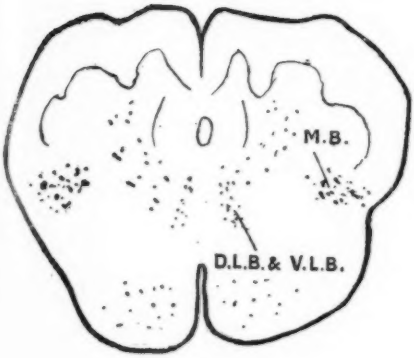
# PLATE XVIII.




Abscess of the mesencephalon. Degeneration in both dorsal longitudinal bundles, both ventral longitudinal bundles, both central tegmental tracts, both brachia conjunctiva; both descending trigeminal roots, both Monakow's bundles and in both mesial fillets.

Degeneration in a tract on either side running from the superior medullary velum to Deiters's nucleus. *Projection drawings.*

PLATE XIX.

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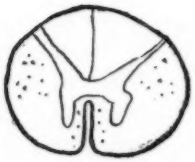

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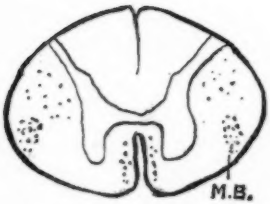


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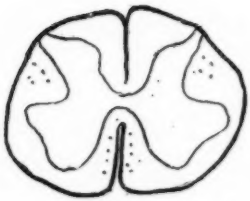

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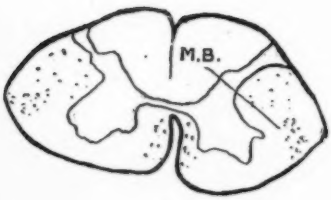


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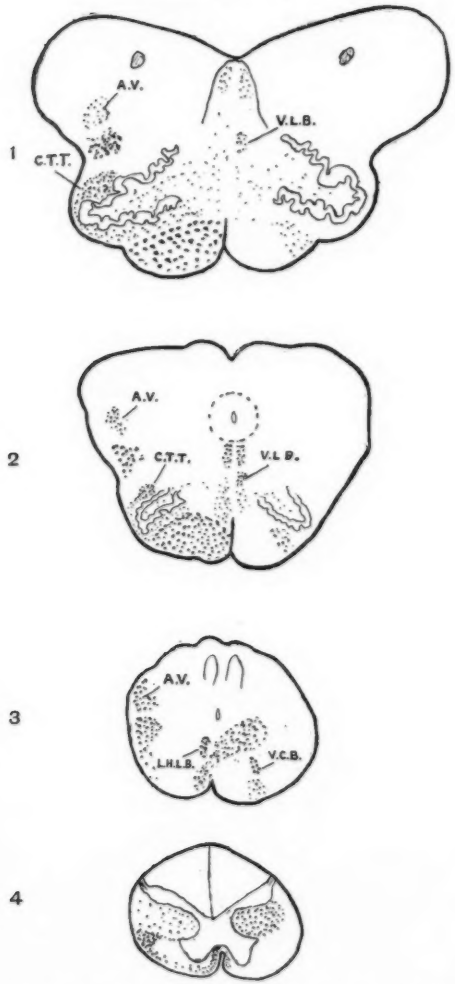
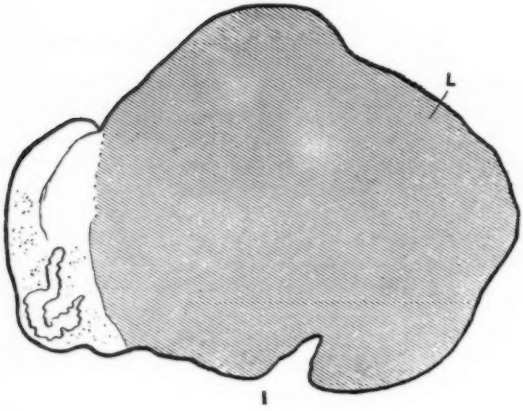
PLATE XX.

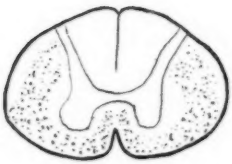


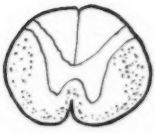

Tumour of the pons extending from the region of the inferior colliculi to the junction of the pons and medulla, more extensive upon the left side.

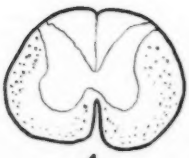
Descending degeneration in both pyramids L. > R., in the left mesial fillet and central tegmental tract, left fasciculus proprius of the medulla, in both dorsal and the R. ventral longitudinal bundle, L. spinal trigeminal root. Atrophy of the left inferior olive. *Projection drawings.*

PLATE XXI.



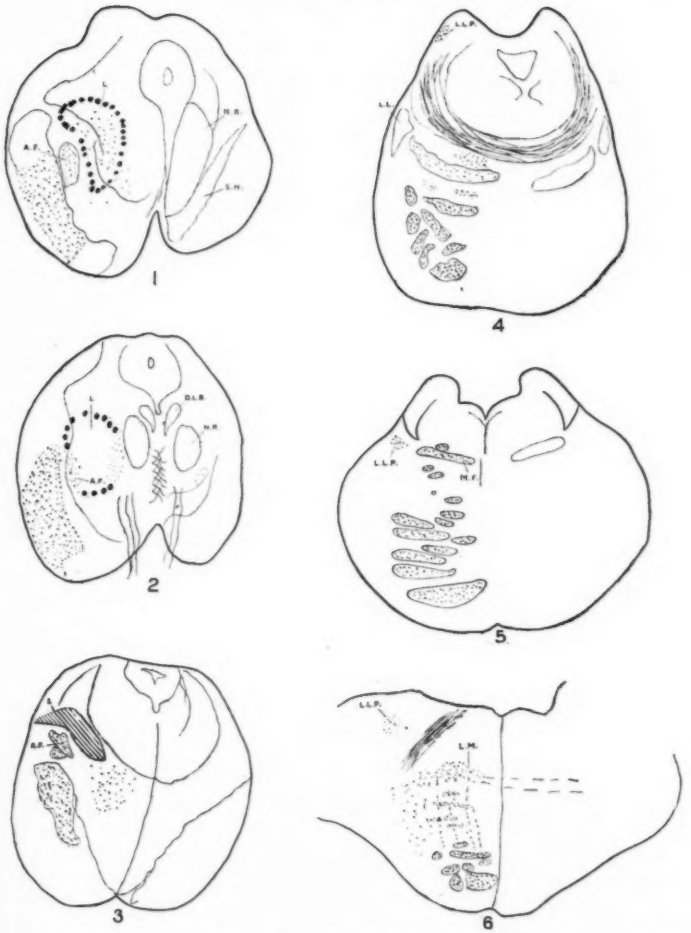




Tumour of the pons and upper medulla with practically complete destruction of the lower pons.

Degeneration in both ventral columns, both antero-lateral columns, and both lateral columns; the direct cerebellar tract and Gowers's tract alone escaping. *Projection drawings.*

# PLATE XXII.

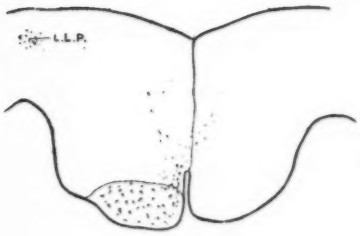



Tumour of left centrum ovale involving the left internal capsule. A localised patch of recent softening was present in the superior collicular region involving the nucleus lateralis superior, the upper part of the substantia nigra, the upper fillet and slightly the outer side of the red nucleus on the left side. A small hæmorrhage was present in the posterior inferior part of the left inferior colliculus.

Degeneration below the lesions in the left pyramidal tract, accessory fillet and masial fillet.

From the lesion in the inferior colliculus a large fibred tract descended having a dorso-lateral situation in the pons and medulla, and in part joining the pyramid at the decussation, appeared to run as a ventro-lateral tract in the cord. *Projection drawings.*

## PLATE XXIII.

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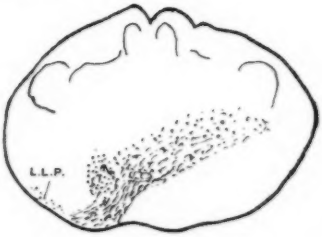


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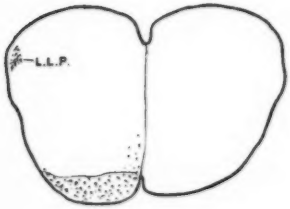


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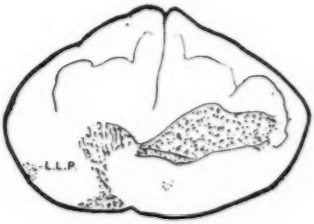


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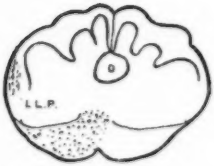


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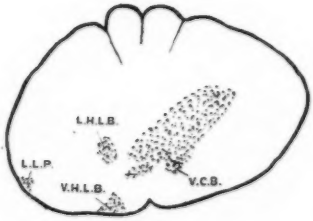


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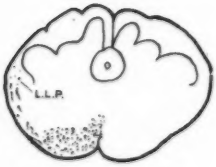


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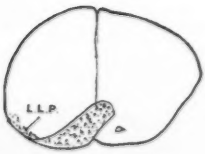


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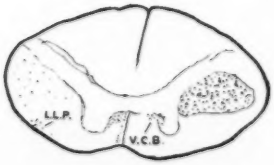


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# PLATE XXIV.

Transverse section of tegmental region of the upper pons showing the ventral longitudinal bundles and the central tegmental tracts. Normal human brain. Pal method.

described by Russell, *i.e.*, crossed and uncrossed ventral and lateral bundles. The course of the accessory fillet corresponded with Bechterew's and with Schlesinger's description except that many fibres appeared to rejoin the pyramid in the pons and medulla. Spitka's bundle (mesial accessory fillet) was not involved.

The tract of fibres from the region of the inferior colliculus is of peculiar interest and will be discussed later. Notwithstanding the lesion of the nucleus lateralis superior and red nucleus there was no degeneration in the ventral longitudinal bundle, nor in Monakow's bundle. Possibly this lesion was too recent to cause evident degeneration.

The foregoing observations bring forward little that is new, but they serve to bring together certain opinions of eminent investigators concerning the origin and destination of some descending mesencephalic tracts, which have hitherto been at variance. The presence of these tracts in man, which have been mostly investigated in animals, and their similarity of origin and course, have received but little attention in this country, and this fact will, we hope, justify the publication of these scanty observations preliminary to a more lengthy investigation upon this subject which it is our intention to pursue.

The points of interest in our observations may be summed up as follows:—

*Monakow's bundle.*—This tract, composed of large fibres, follows an almost identical course already described in the cat, monkey, and in man. It is relatively a large tract in the cat, relatively a small tract in man. So far as the descending fibres of this tract are concerned they appear to cross entirely in Forel's decussation. The majority of the fibres appear to have their origin in the caudal part of the red nucleus. Probst has recently found that wherever the red nucleus is injured degeneration in this tract follows, and that a lesion of a mesencephalon not involving the red nucleus gives rise to no degeneration of this tract. Our observations do not accord with his results. In experiment 5 and in case No. 5 the anterior and lateral aspect of the red nucleus respectively were injured and Monakow's bundle

showed no degeneration. This suggests that the cells of the caudal part of the nucleus only give rise to the fibres in question. Further we have, beyond all doubt, traced fibres from the gray matter lying immediately ventro-lateral to the dorsal commissure, across Forel's decussation into Monakow's bundle and this in a case where there was no degeneration in the ventral longitudinal bundle of the crossed side. This origin for the fibres of Monakow's bundle was suggested by Held, Nissl and Boyce, while the majority of writers on the subject consider the red nucleus only to be the place of origin of the descending fibres of this tract. Our observations incline strongly in favour of a double origin for the fibres, the majority arising in the cells of the red nucleus, others in the gray matter close to the dorsal commissure. The latter fibres appear to cross just at the junction of Meynert's and Forel's decussations.

In more than one of our experiments a few fibres appeared to leave this tract as it lay in the fasciculus proprius medullæ and to run to the cerebellum with the restiform body. Such fibres have not, so far as we are aware, been described by other observers; they were the only fibres leaving the tract above the pyramidal decussation. In the cat, monkey, and man we have traced the tract into the sacral region, its termination in the ventral horns of the same side being easily seen. Only above the dorsal region were the fibres distinctly separated from those of the lateral pyramidal tract, lying in front of the latter.

The lateral ponto-spinal tract occupies apparently the same position in the medulla and spinal cord as does Monakow's bundle. Comparing the low pontine lesion in case 3 with the mesencephalic lesions in cases 1 and 2, the much greater degeneration in the fasciculus proprius medullæ and in the position occupied by Monakow's bundle in the cord in the former case is obvious. In this case the pontine nuclei and Deiters's nucleus of the left side were destroyed, and the large area of degeneration ventral to the spinal root of the fifth on the left side represents the combined lateral tract from the mesencephalon, pons, and upper medulla. Traced into the spinal cord, the degeneration in case 3

spread out in a band reaching from the lips of the ventral fissure nearly to the mid-point of the lateral column, and in the lateral column formed a wedge-shaped tract with base to the surface and apex stretching towards the lateral horn. Below the cervical region that part of the degeneration forming the wedge merged gradually into the lateral pyramidal tract (lateral ponto-spinal and rubro-spinal fibres), but the degeneration stretching along the surface outwards from the lips of the ventral fissure retained this position as long as it was traceable, that was to the lower dorsal region (vestibulo-spinal fibres).

The *ventral longitudinal bundle* is described as having its origin in the nuclei lateralis superior and centralis superior and as crossing entirely in the fountain crossway. We have not actually traced the degeneration from the nucleus lateralis superior, but have found marked degeneration of the bundle where this nucleus was intact. In most of our cases the fibres evidently arose from the gray matter immediately ventro-lateral to the dorsal commissure and having a curved course round the gray matter encircling the aqueduct, crossed in the fountain crossway. We can firmly support Held's statement that some of these fibres do not cross, but enter the ventral longitudinal bundle of the same side.

The crossed relation of the degeneration of the dorsal longitudinal bundle with that of the ventral longitudinal bundle and Monakow's bundle in unilateral lesions of the mesencephalon is striking, and is explained by the fibres of the dorsal longitudinal bundle being involved by such a lesion after they have crossed in the dorsal commissure.

The position of this tract as regards its proximity to the raphe of the pons and medulla seems to vary considerably. In the cord the fibres are spread out along the sides of the ventral fissure. We have traced them to the lumbar region.

The *vestibulo-spinal tract* must have been involved in cases 3 and 4, and the degeneration in the spinal cords of these cases involves an area amongst other degenerate areas quite corresponding with the classic description of the fibres

descending from Deiters's nucleus to the spinal ventral horns. These fibres were traceable to the sacral regions of the spinal cord.

The above tracts, Monakow's bundle, the ponto-spinal tract, and vestibulo-spinal tracts, and some fibres of the dorsal and ventral longitudinal bundle, may be considered together as constituting a system descending from the various lower levels of the brain and probably constituting an alternative path by which motor impulses reach the spinal cord, the other path being the pyramidal system. In birds there is no direct descending path from the cerebrum, and, according to the investigations of Münzner and Wiener, Monakow's bundle is in these animals very well developed. In mammals the tracts here considered are well developed, it would seem, inversely to the development of the pyramidal system. In no case have we found so many fibres, for instance in Monakow's bundle in man, as in the cat. This inverse proportion of the development of these tracts and the pyramidal system is interesting in connection with the well-known persistence of voluntary movement after destruction of the pyramidal systems in lower mammals. Starlinger, Wertheimer and Le Page have shown that complete destruction of the pyramidal fibres at the decussation abolishes neither voluntary movement nor movements of the limbs as a result of cortical stimulation in the dog and monkey. Stoddart also proved that cortical excitation produced movements of the hind limbs and tail after longitudinal section of the decussation. It seems probable that the tracts here concerned represent the original paths for impulses from higher to lower parts in the nervous system, and that the path from cerebrum to cord, at first indirect, has with the process of evolution become direct by the development of a short circuit system—the pyramidal system—running direct from cerebral cortex to the lower levels. It has further been stated that no case has ever been brought forward in man in which complete destruction of the pyramidal tracts of one side below the thalamus has been followed by complete paralysis.

In connection with decerebrate rigidity and the presence

of the deep reflexes in transverse lesions of the nervous system we may point out that when, as in Sherrington's original experiments, decerebrate rigidity is produced by mesencephalic transection in the cat, if hemisection of the medulla or cord be subsequently performed, such rigidity disappears at once on the side of and caudal of the hemisection. We suggest that the efferent paths essential for the production of decerebrate rigidity may be some of the tracts here concerned.

The integrity of the connection of the higher with the lower parts of the nervous system is now generally considered in man to be essential for the production of the deep reflexes. Total transverse lesions of the spinal cord abolish them. In connection with the disease "acute combined sclerosis" in which there is a progressive degeneration of all the long fibre systems in the spinal cord, the clinical aspect of the disease is, at first, one of spastic paraplegia, and subsequently if the patient live, one of flaccid paraplegia with absence of the deep reflexes. We would suggest, as the result of the pathological condition found by one of us (J. C.) in twelve cases, seven of which were published in this journal by Dr. Russell and Dr. Batten, that the onset of flaccid paralysis and loss of the deep reflexes is coincident with the degeneration of the remaining descending long fibres systems in the cord; for the pyramidal system suffers early in this disease and the short fibres systems have never been extensively affected. The afferent tracts are affected earliest of all in the disease and they have been found completely degenerate where spasticity continued to the end. It would seem to us then that the integrity of the long fibres systems of the antero-lateral regions of the cord dealt with in this paper, and which are among the last to be involved in combined degeneration is responsible for the maintenance of rigidity and the deep reflexes in default of the pyramidal systems and that with their degeneration flaccidity sets in and the deep reflexes are no longer obtainable.

We are promised the results of a wide experimental investigation into the physiology of these tracts at an early date by Rothmann.

It was pointed out as long ago as 1866 by Bouchard in cases of hemiplegia that the area of degeneration in transverse sections of the cord varied with the position of the lesion causing the hemiplegia. He showed that where the lesion implicated the hemisphere only the degeneration in the lateral column was sharply marked off ventrally, but that where the mesencephalon and pons were implicated the area of degeneration spread forwards towards the ventral roots and that the lower the lesion in the brain stem the more the degenerated area encroached upon the antero-lateral column. Many authors have since confirmed this fact, and indeed from the area of degeneration in sections of the cervical cord in such cases it is possible to infer with considerable accuracy the position of the lesion in the brain.

The *central tegmental tract* as degenerating caudalwards in lesions of the brain stem has been a most striking feature in three of the cases recorded here, and a few of its fibres were degenerated in one of the monkeys. In the other experiments the position and sagittal direction of the lesions probably explain the absence of degeneration of this tract.

We have found its course exactly as described by Bechterew, but our cases did not afford an investigation of its origin further than the fact that it was not degenerated in the cat in a lesion of the dorso-mesial part of the thalamus.

Most of the fibres of the tract appeared to end on the surface of the inferior olive of the same side, but some running between the pyramid and the olive appeared to enter the hilum olivæ and some seemed to be lost in the interolivary layer. As, however, in each of our cases where the central tegmental tract was degenerate, descending fibres of the fillet were degenerate in the interolivary layer, we were unable to trace with certainty the fibres of the central tegmental tract in the interolivary layer. We were unable to trace any of the fibres into Helweg's triangular tract.

In the *Neurologische Centralblatt* for June 16, 1901, Professor Obersteiner publishes a case of tumour of the dorsal aspect of one half of the medulla in which he figures what he considers to be degeneration in the triangular field

and traces this to the upper thoracic region of the spinal cord. He considers this tract to arise above the olive and to have no connection with the central tegmental tract which he considers to end in and upon the olive. We would point out, however, that the degeneration he figures corresponds exactly with that of the vestibulo-spinal tract, with perhaps some fibres of the rubro-spinal and ponto-spinal tracts. From his figure the former must have been implicated in the lesion, and the latter possibly. He figures a coarse fibre degeneration which, he admits, is not in the recognised position of the triangular path, and traces it to the dorsal region. The triangular path is, however, composed of very minute fibres. We cannot think that his interpretation of this case is clearly proved, nor that his dissent, on the grounds of his case, from von Bechterew's assertion upon the origin of the triangular path in the inferior olive (fasciculus periolivaris), logical.

In two of our cases there was marked atrophy of the inferior olive. This atrophy seemed to depend upon the degeneration of the central tegmental tract and not upon that of the fillet. This atrophy has been noted by Mott and others after hemi-transection of the brain stem and has been usually considered a disuse atrophy resulting from a lesion of the mesial fillet.

The descending fibres of the fillet seem to fall into at least three groups. Firstly, those fibres which descend doubtless from the pyramidal radiation from the accessory fillet of von Bechterew (lateral pontine bundle of Schlesinger) lie at first as scattered bundles in the substantia nigra, close to the dorso-mesial aspect of the crusta, and which subsequently enter the mesial fillet to be distributed to the nuclei of certain cranial nerves (coarse fibres of late myelination). Secondly, fine fibres of the mesial fillet which in the cat and monkey degenerate downwards after lesions of the thalamus and upper fillet, and can be traced for a certain distance only, apparently becoming lost in the reticular formations of the pons and medulla. Lastly, in old standing lesions at least, a great many fibres of the mesial fillet degenerate below lesions and can be traced through the interolivary

layer, some to the olivæ and some through the fillet decussation to the posterior column nuclei. In cases where the mesial fillet has been destroyed the number of fibres which behave in this way is so great that the degeneration is plainly visible by the Pal method.

In case 5, the *accessory fillet* was entirely degenerated upon one side; it was traced from the capsule, and the degenerate fibres were seen to enter the motor nucleus of the fifth of both sides and the nucleus of the facial nerve on both sides and also the nucleus of the hypoglossal on both sides, but neither the nuclei oculo-motorii, abducentes, nor vagi. Many of these fibres seemed to re-enter the pyramid in the region of the medulla.

The fibres of the second class were met with in some of the experimental lesions and in case 5. Apparently they were fine fibres with origin above the mesencephalon, running down in the region of the upper and subsequently the mesial fillet, and becoming scattered and finally lost in the reticular formation of the pons and medulla.

The third group of fillet fibres were degenerated in all the cases where the middle fillet was injured. Such degeneration has been referred to by many authors as "retrograde degeneration." However, this degeneration may be most obvious in so short a time as eight weeks after the lesion, as we have noticed in more than one case in the human subject (not reported here), and is in no way that we are aware of to be distinguished from ordinary degeneration. It may be argued that this degeneration of the fillet is of the same nature as is the posterior root and posterior column degeneration which occurs in connection with cerebral tumour and vascular lesions of the brain, whatever the nature of the process. If such argument be valid the degeneration is an ascending one. The posterior degeneration is, however, independent of the location of the lesion, whereas the descending fillet degeneration is consequent only, so far as we are aware, upon an implication of the tract itself.

The tract descending from the region of the inferior colliculus in case 5 is peculiar. Its course, outside the superior brachium and restiform body in the lateral part of

the pons and subsequently on the dorso-lateral aspect of the restiform body, was remarkable.

Moreover it was separated off anatomically in the region of the restiform body as a rounded bundle and could plainly be seen on the non-degenerate side. We have searched through a number of specimens of this region stained by Pal's method from different cases and have as yet failed to find any similar tract separated off from the restiform body. It was composed of large fibres and in part seemed to join the pyramid just above the decussation, in part ran in the ventro-lateral region of the spinal cord. The fibres joining the pyramid seemed continued into the uncrossed ventral pyramidal tract.

We are unaware of any previous description of such a tract. From its mode of termination and from the fact that it was degenerated upon the side of a complete pyramidal degeneration, we would suggest that it was an aberrant pyramidal bundle, though its widely lateral course in the pons is not in line with this suggestion. From the position of the hæmorrhage in the inferior collicular region it was impossible to trace its upper connection with the pyramid if such existed.

*The Tracts from the Nuclei Fastigii to Deiters's Nuclei.*

The degeneration in case 2 shows that some of the constituent fibres are cerebellofugal. We were unable to trace any of these fibres to the nucleus of the vagus.

*Fibres descending from the Thalamus to the Ventral Columns.*

In experiment 5 (cat) a well-marked bundle of fibres descended from the thalamic region to the ventral column having an uncrossed course and being situated ventro-lateral to the ventral longitudinal bundle. They were not fibres of the fillet system, being always situated in a position ventral to the latter. They did not correspond with Held's uncrossed fibres of the ventral longitudinal bundle since their origin was in the deep part of the thalamus and their course not that of the ventral longitudinal bundle. Some of these fibres were traced in the ventral column of the cord close to the fissure to the lowest cervical region.

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## EXPLANATIONS OF ABBREVIATIONS IN FIGURES AND PHOTOGRAPHS.

*A. C. Q.*—Anterior corpus quadrigeminum.
*A. F.*—Accessory fillet.
*A. V.*—Spinal root of 5th.
*A. L.*—Ansa lenticularis.
*B. C.*—Brachium conjunctivum.
*C. T. T.*—Central tegmental tract.
*C. S.*—Corpus subthalamicum.
*C. F.*—Columns of fornix.
*C. R.*—Corpus restiforme.
*D. L. B.*—Dorsal longitudinal bundle.
*D. B. C.*—Decussation of brachia conjunctiva.
*D. B.* 6.—Fibres from dorsal longitudinal bundle to opposite 6th nucleus.
*D. F. F.*—Descending fillet fibres.
*D. V.*—Descending root of 5th.

*D. F.*—Decussation of fillet.
*D. P.*—Decussation of pyramids.
*D. C. T.*—Direct cerebellar tract.
*F. D.*—Forel's decussation.
*F. R.*—Fasciculus retroflexus.
*H. C.*—Habenular commissure.
*I. C.*—Internal capsule.
*L.*—Lesion.
*L. F.*—Lateral fillet.
*L. H. B. L.*—Lateral homolateral bundle of pyramid.
*L. L. P.*—Bundle from inferior collicular region to ventral column.
*M. D.*—Meynert's decussation.
*M. B.*—Monakow's bundle.
*M. F.*—Mesial fillet.
*M. C.*—Middle commissure.
*N.* 3.—Nervus oculo-motorius.
*N.* 4.—Nervus trochlearis.
*N.* 5.—Nervus trigeminus.
*N.* 6.—Nervus abducens.
*N.* 7.—Nervus facialis.
*N.* 8.—Nervus auditorius.
*N. L.*—Nucleus lenticularis.
*N. L. M.*—Nucleus lateralis medullæ.
*N. R.*—Nucleus ruber.
*O.*—Inferior olive.
*O. T.*—Optic tract.
*P.*—Pyramid.
*P. C. Q.*—Posterior corpus quadrigeminum.
*P. C.*—Posterior commissure.
*S. O.*—Superior olive.
*Th.* O.—Optic thalamus.
*V. C. B.*—Ventral crossed bundle of pyramid.
*V. H. L. B.*—Ventral homolateral bundle of pyramid.
*V. L. D.*—Ventral longitudinal bundle.
*V. S.*—Vestibulo-spinal tract.
*Y.*—Fibres from thalamus to ventral column.

# DEGENERATIONS FOLLOWING A TRAUMATIC LESION OF THE SPINAL CORD, WITH AN ACCOUNT OF A TRACT IN THE CERVICAL REGION.

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THE case upon which the following paper is based was that of a female patient, aged 28, in the Westminster Hospital, who sustained a dislocation of the vertebral column between the bodies of the 5th and 6th cervical vertebræ, crushing the spinal cord at the upper part of the 7th segment for a vertical extent of about half an inch. The patient survived for ten weeks after the injury. The clinical aspects of the case have been dealt with in a former article in this Journal.[1]

The whole spinal cord, the medulla oblongata and the pons Varolii were obtained for examination. Sections of the pons, medulla and cord were stained by the Marchi method, together with the anterior and posterior nerve-roots of both sides from the 5th cervical to the 1st thoracic inclusive. The segments of the cord in the vicinity of the lesion, both above and below, were stained by the Thionin-Nissl and by van Gieson's hæmatoxylin and picro-fuchsin methods; segments from the mid-thoracic and mid-lumbar regions were also examined by the latter methods.

I desire here to express my indebtedness to Dr. Ferrier and to Dr. Batten for their courtesy in permitting me to prepare the sections in the Neuro-pathological Laboratory, King's College, and in the laboratory of the National Hospital, Queen Square, respectively.

[1] BRAIN, 1900, vol. 23, pp. 139-156.

## Extent of Lesion.

At the upper part of the 7th cervical segment the cord was abruptly flattened to a thin ribbon, measuring only 1mm. in antero-posterior thickness. Below that level there were hæmorrhages within the cord, extending, on the right side, through the gray matter and in the ventral part of the posterior column as low down as the lower part of the 8th cervical segment, and on the left side to a similar situation as far as the lower part of the 7th cervical segment: no hæmorrhage extended upwards on the cephalic side of the lesion beyond the immediate vicinity of the injury. None of the nerve-roots, anterior or posterior, were torn across. On examination of the *anterior nerve-roots* on both sides, from the 3rd cervical to the 1st thoracic inclusive, the *7th cervical pair* were alone found degenerated. All the corresponding posterior nerve-roots of both sides were quite free from degeneration in their extra-medullary course, as shown by the Marchi stain.

## Explanation of Illustrations.

In the case of the spinal cord it should be noted that the most caudal part of every segment, from the uppermost cervical to the coccygeal, was systematically chosen for examination. In the medulla and pons thin slices were examined at short distances from each other. In every instance the section was magnified ten times and traced by means of Edinger's projection apparatus and the degenerations accurately filled in, partly under the projection apparatus and partly by comparison with the aid of the microscope. In this way a complete series of figures was obtained, illustrating the degenerations which had supervened in the various tracts. The figures were again photographed down to their present size.

We shall consider the degenerations in the following order:—

## Descending Degenerations.

(*a*) Lateral columns.
(*b*) Anterior columns.
(*c*) Posterior columns

ASCENDING DEGENERATIONS.

(*d*) Posterior columns.
(*e*) Antero-lateral columns.

(*a*) *Descending Degenerations of Lateral Columns.*

(1) *Lateral pyramidal tract.*—This can be traced from the level of the lesion down to the lowest part of the coccygeal segment. At the level of the upper sacral region the number of its fibres rapidly diminishes, but there can be no doubt that it extends to the caudal extremity of the cord. Ludwig Müller[1] has recently maintained that no degeneration is ever found in the lateral columns below the 3rd sacral segment, and v. Bechterew[2] and Ziehen[3] state that the tract terminates about the 3rd or 4th sacral segment. Barker,[4] in his text-book, states that a certain number of fibres can be traced into the lowest portion of the sacral region, whilst Risien Russell[5] and Déjérine and Thomas[6] state that the tract extends to the most caudal extremity of the cord. Our sections are in entire agreement with the statements of the two latter observers.

As low down as the 6th thoracic segment we observe that the outermost fibres of the crossed pyramidal tract do not reach quite to the periphery of the cord. From the 7th thoracic segment, however, down to the coccygeal region, they are adjacent to the lateral surface of the cord. The innermost fibres of the tract throughout the greater extent of the cord lie close against the gray matter, but from the 5th lumbar segment downwards the tract gradually recedes outwards and lies at some distance from the gray matter (see plates 5 and 6).

(2) *Tract "X": ventro-external to the crossed pyramidal tract.*—In the 7th and 8th cervical segments, close to the periphery of the cord, a small sharply-defined, degenerated area can be clearly seen at a plane corresponding to the tip of the lateral horn, ventro-external to the crossed pyramidal tract and separated from the latter by a distinct space (see plates 5 and 7). It has a short course and cannot be traced below the 8th cervical segment. It is closely applied to the

surface of the cord at that portion corresponding to the tip of the lateral horn of the gray matter.

Various descending tracts, in addition to those of the pyramidal system, have been described in the antero-lateral columns of the cord. Thus the vestibulo-spinal or efferent antero-lateral tract, descending from Deiters's nucleus, figured by Ferrier and Turner,[7] Risien Russell,[8] Probst,[33] and others, occupies the peripheral portion of the ventral part of the cord (see figure 1). But our tract is much

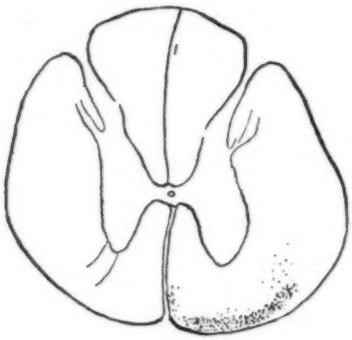


FIG. 1.

Descending tract from Deiters's nucleus. (Probst, *op. cit.*, Tafel vii., fig. 7.

smaller and more compact than the above, and lies farther back, in the lateral column, not in the anterior column as in the case of the vestibulo-spinal tract. Moreover, "tract X" stops short at the lower end of the cervical enlargement, whereas the vestibulo-spinal tract extends caudally as far as the lumbar region.

The position of "tract X," sharply marked off by a distinct gap from the crossed pyramidal tract, also differs from that of the rubro-spinal tract described by Monakow,[29] in the dog, and by Boyce,[9] Held[30] and others in man, which is diffusely scattered through the antero-lateral column and overlaps the area of the crossed pyramidal tract (see figure 2).

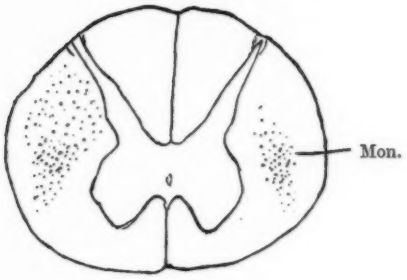



FIG. 2.

Monakow's bundle in the monkey, after a mesial lesion in Forel's decussation. (From a drawing by Dr. James Collier.)

The "triangular pre-pyramidal tract," described by André Thomas[34] in the cat in a case of hemisection of the cord (see figure 3) which is apposed by its base to the crossed pyramidal tract, whilst its apex is directed forwards, is probably identical, as Thomas admits, with Monakow's bundle, and, like it, can be traced to the lumbar region of the cord.

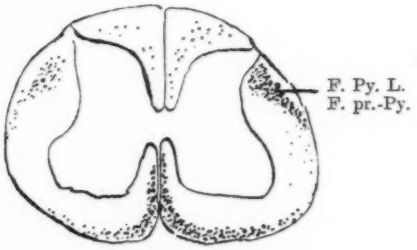



FIG. 3.

"Faisceau triangulaire pre-pyramidal," described by André Thomas (*op. cit.*, p. 49, fig. 3). Level of 7th cervical segment (cat).

(Monakow's bundle is more fully discussed by Buzzard and Collier in another article in this number of BRAIN, to which they have courteously allowed me access while their paper is going through the press.)

The descending tract from Bechterew's nucleus reticularis in the pons and which, in the cord, is situated close to the anterior median fissure—"Fissurenstrang" of Tschermak—only requires to be mentioned to show that it is in no way related to the tract now under consideration.

A tract corresponding somewhat more closely in position to the "tract X" is that described by Helweg[10] as the "triangular tract," and independently by von Bechterew[11] as the "olivary tract." Helweg's tract, however, lies more anteriorly than "tract X" (see figure 4). It has been a

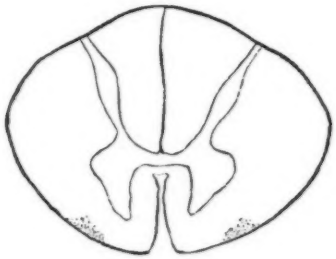


FIG. 4.

Helweg's tract at the level of the 3rd cervical segment. (From "Bruce's Atlas of the Spinal Cord.")

disputed point whether Helweg's tract is centrifugal or centripetal; Obersteiner[25] admits that the evidence is inconclusive one way or the other; Reinhold[12] claims to have traced Helweg's tract, although only by the Weigert-Pal method, in a case of melancholia, to the mid-thoracic region; but Bruce,[31] in his recent atlas, does not find it below the 3rd cervical segment, and Meyer[13] also traces it only to the 3rd cervical segment, after hardening by Müller's fluid, in a case of pontine hæmorrhage. Both Reinhold and Meyer incline to the view that it is a descending tract, which is suggested by Reinhold to be vasomotor in function. On the other hand, von Bechterew,[11] after originally stating that Helweg's tract arises "undoubtedly" from the cells of the lateral horn, proceeds in a more recent paper[11A] to explain that this is

merely a "topographical" expression, and that the tract is really a descending one. Edinger[14] regards Helweg's tract as an ascending one. "Tract X," however, is a descending one, and it stops short at the lower end of the cervical enlargement. Further, its position, at a plane corresponding to the tip of the lateral horn, differs from that of Helweg's tract, which lies among the anterior nerve roots. Moreover, its degenerated fibres do not differ in average calibre from those of the crossed pyramidal tract, whereas both Helweg and von Bechterew agree that the "Olivenstrang" or "Dreikantenbahn" is made up of very fine fibres. Probably, however, the recent degeneration in our case renders the measurement of its individual fibres of less importance, since nerve-fibres may become considerably swollen during the process of degeneration.

On the whole, then, we may conclude that "tract X" is a descending tract which does not correspond in position to the "Dreikantenbahn" or "Olivenbündel" of Helweg and von Bechterew, and that, unlike the latter, it terminates at the lower end of the cervical enlargement.

The possibility of "tract X" being an aberrant strand of the pyramidal system must also be borne in mind. In a case such as ours, however, such a hypothesis is incapable of proof or disproof.

(*b*) *Descending Degenerations of Anterior Columns.*

(1) *Ventral pyramidal tract.*—This can be traced as a distinct band of degeneration, bounding the anterior median fissure in its whole depth, as far caudally as the 3rd lumbar segment. Below that level the ventral fibres of the tract become scanty and the part which extends farthest in a caudal direction is that portion which lies close to the bottom of the fissure. This latter portion of the tract can be traced as low as the lower part of the 4th sacral segment, below which level, although there are a few scattered degenerated fibres in the anterior columns, they can scarcely be dignified any longer by the name of a distinct "tract" (see plate 6).

This tract is said by Barker[4] and by Ziehen[15] to end usually in the mid-thoracic region, though both of these

authors admit with Tooth[16] that in rare cases it may be followed to the middle of the lumbar enlargement. Dejerine and Thomas,[6] however, trace it to the 4th sacral and Risien Russell[5] to the 5th sacral segment. Our case is again in agreement with the three latter observers.

(2) *Efferent ventro-lateral tract.*—The fibres of this tract are known to be derived from various sources. Upon the discussion of these sources, the present case, being due to a bilateral spinal lesion, throws no light. The tract is seen to occupy the extreme periphery of the ventral portion of the cord from the anterior median fissure outwards. As low down as the 4th lumbar segment it is seen to be in close apposition with the ventral pyramidal tract. Below that level, as the ventral pyramidal tract shrinks towards the deepest part of the anterior median fissure, the efferent ventro-lateral tract remains close to the surface of the cord and can be traced as a distinct path as far as the lower part of the 4th sacral segment. Below the 4th sacral, scattered degenerated fibres are diffusely dotted over the whole ventral part of the cord.

As we trace this tract downwards it extends less and less outwards towards the lateral aspect of the cord; the part which extends farthest caudally being that which lies near to the anterior median fissure (see plate 6).

(3) *Fibres in anterior commissure.*—Degenerated fibres can be traced in the "commissura alba" for three segments below the lesion, as far down as the lower part of the 1st thoracic segment. Below that level the anterior commissure is free from degeneration.

(*c*) *Descending Degenerations of Posterior Columns.*

"*Comma*" *tract* of Schultze; *septo-marginal tract* of Bruce and Muir; *centrum ovale* of Flechsig and *triangle médian* of Gombault and Philippe (see plates 5 and 6).

The "comma" tract of Schultze forms a well-marked stripe of degeneration in the postero-external column of each side, extending from the dorsal aspect of the gray commissure in front to the posterior surface of the cord behind. This appearance of the tract is maintained, though its fibres

gradually diminish in number from above downwards, as far caudally as the 9th thoracic segment. Below this level, the ventral part of the tract disappears, whilst its superficial, most dorsal portion continues to run on caudally as the "septo-marginal" tract, whose fibres at the level of the 10th thoracic segment begins to bend inwards, along the dorsal surface of the cord, towards the median septum. At the 11th thoracic segment they form a thin layer bounding the dorsal surface of the postero-internal column. In this position they run caudally for three segments (Th. 11 and 12 and L. 1). At the 2nd lumbar segment they turn the corner and dip ventrally inwards into the posterior median septum. At the 3rd, 4th and 5th lumbar segments the fibres lie close to the median septum, and at a little distance from the dorsal surface, the tracts of the two sides here forming the "oval field" of Flechsig. At the 1st sacral segment the dorsal margin of the tract again reaches the surface, and from this level it can be traced in a caudal direction down to the lowest part of the coccygeal region. From the 3rd sacral segment downwards the tracts of the two sides form a triangular area (*triangle médian* of Gombault and Philippe) whose base is situated at the dorsal surface and whose apex extends for a short distance into the posterior median septum.

Hoche, in his classic paper,[17] states that the "comma" tract is entirely separate and distinct from the combined bundle composed of the septo-marginal tract, the centrum ovale, and the triangle médian; in which view he is supported by Barker,[18] who designates them as "two distinct and now fairly sharply defined descending tracts," and by Dejerine and Theohari,[19] who also regard Schultze's comma tract as an entity anatomically independent of Hoche's peripherally situated bundle. Our case, however, tends to show that no line of demarcation can be drawn between these various bundles of descending fibres, and that they may reasonably be considered as forming, not two, but one long continuous system. Nageotti and Ettlinger,[28] from a study of two cases of transverse lesion in the dorso-lumbar region, also come to this conclusion, which is also supported

by Janischewsky's [32] case of lesion in the 7th cervical segment. The question as to which fibres of this system are endogenous and which exogenous in origin is not elucidated by our case, inasmuch as the lesion was one which destroyed both endogenous and exogenous fibres at the level of injury.

(2) *Short descending fibres near median septum.*—In addition to the combined system of tracts already described, our sections show, as in Hoche's case, another group of descending fibres in the dorsal funiculi of the cord, lying along the posterior median septum about its middle, but not extending farther down than the 8th cervical segment. These fibres are evidently short ones, distinct from those of the "comma" tract.

Finally, a number of degenerated fibres lie scattered diffusely over the whole field of the posterior columns, and most abundantly near the dorsal surface of the postero-internal columns. They also stop short below the 8th cervical segment, and may probably be fairly included within the limits of "traumatic" degeneration.

### (*d*) *Ascending Degeneration of Posterior Columns.*

At the 5th cervical segment, the posterior columns show well-marked degeneration over their entire area, except in a limited portion of the postero-external column in the vicinity of the posterior horn where a number of undegenerated fibres are situated, having entered the cord through the posterior nerve-roots of the 6th cervical segment, above the level of the lesion. With this exception, the degeneration occupies the whole area of the posterior columns from the dorsal surface to the gray commissure, forming a wedge-shaped area whose apex points ventrally and is embedded in the concavity of a crescentic area of degeneration situated close to the gray matter—the "cornu-commissural zone" of Marie. Above the 2nd cervical segment this cornu-commissural crescent disappears, and at the lower end of the 1st cervical segment the wedge alone survives, its apex touching the gray commissure. The base of the wedge at this level lies both in the postero-external and postero-

internal columns: its apex lies in the postero-internal columns only (see plate 4).

Sections through the lower and upper parts of the pyramidal decussation and through the lower end of the inferior olive show the blunting of the apex of the wedge by the gradual pushing backwards of the gray matter towards the dorsal surface, and the appearance, first of the nuclei graciles and then, at a higher level, of the nuclei cuneati, into which nuclei, but especially the cuneate, most of the degenerated fibres are traced (see plate 3).

But the degeneration does not cease abruptly at the posterior column nuclei. Distinct degeneration can be seen higher up, in the arcuate fibres of the medulla, both in the postero-external arcuate fibres, on the surface of the medulla, and in the decussating internal arcuate fibres. By the time the level of the lower end of the 4th ventricle is reached this degeneration of the arcuate fibres is less conspicuous and is seen chiefly in the vicinity of the raphé. In this respect our sections entirely corroborate the results of Hoche,[17] Schaffer[20] and others, although both Mott[23] and Sherrington[24] in experimental degenerations produced in monkeys failed to find degenerated fibres above the posterior column nuclei.

(*e*) *Ascending Degeneration of Antero-lateral Columns.*

(1) *Dorso-lateral, or direct, cerebellar tract.*—At the 5th cervical segment this forms a flat narrow strip at the periphery of the dorsal part of the lateral column. Its anterior margin abuts closely on the adjacent ascending antero-lateral tract, which is also degenerated. At the level of the pyramidal decussation the dorso-lateral cerebellar tract comes to form a somewhat wedge-shaped area occupying the angle between the substantia gelatinosa and the lateral surface of the cord. As we trace it higher, its fibres recede still farther dorsally and run external to the substantia gelatinosa to enter the corpus restiforme and go to the cerebellum (see plates 3 and 2).

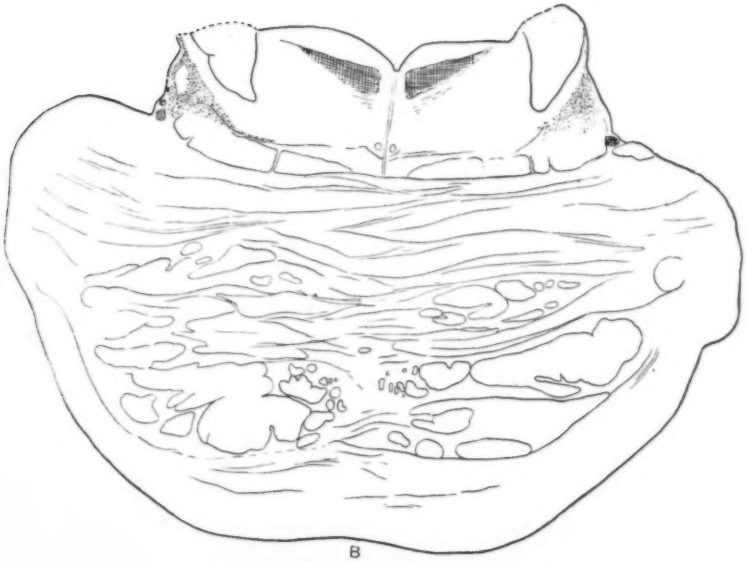
(2) *Ascending antero-lateral tract* (*Gowers*).—The head of the "comma," situated dorsally, close to the previous

# PLATE 1.

## Ascending Degenerations.

A

Level of valve of Vieussens.

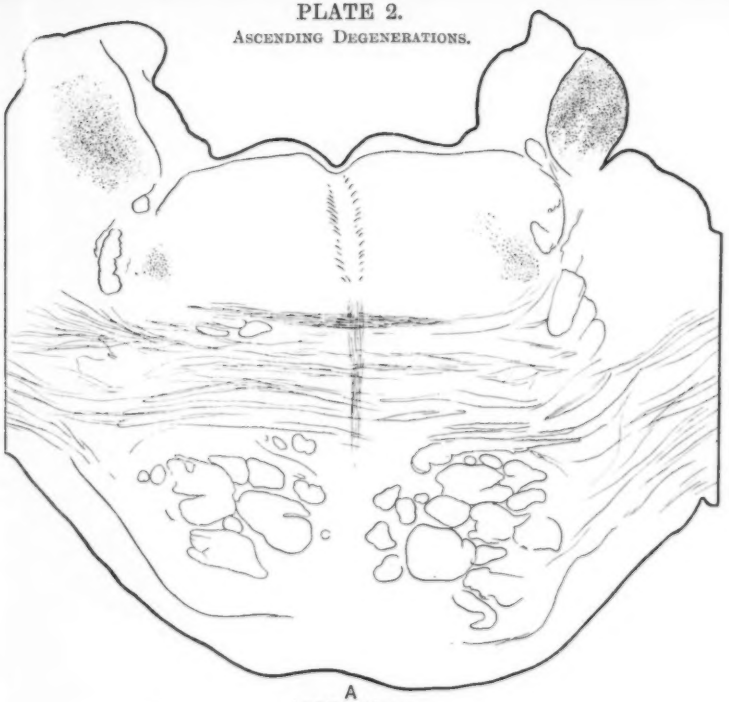


B

Upper part of pons.

# PLATE 2.

## Ascending Degenerations.



A

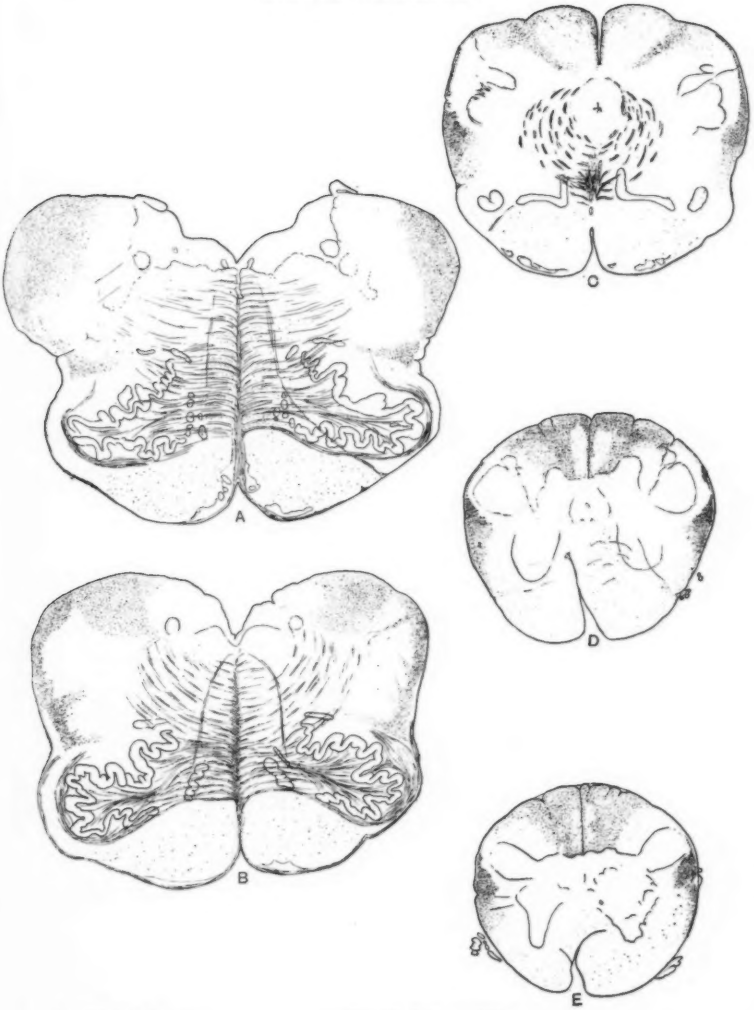
Middle of pons.

B

Level of facial nerve.

## PLATE 3.

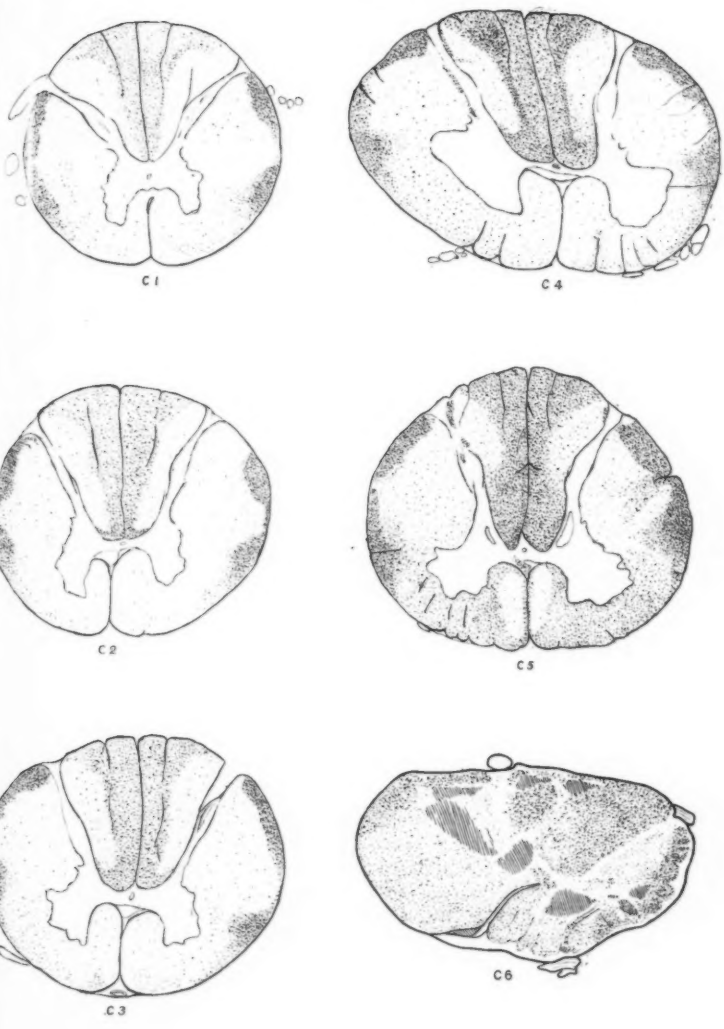
ASCENDING DEGENERATIONS.




*A.*—Medulla, upper. *B.*—Medulla, middle.
*C.*—Medulla, lower. *D.*—Pyramidal decussation, upper part.
*E.*—Pyramidal decussation, lower part.

# PLATE 4.

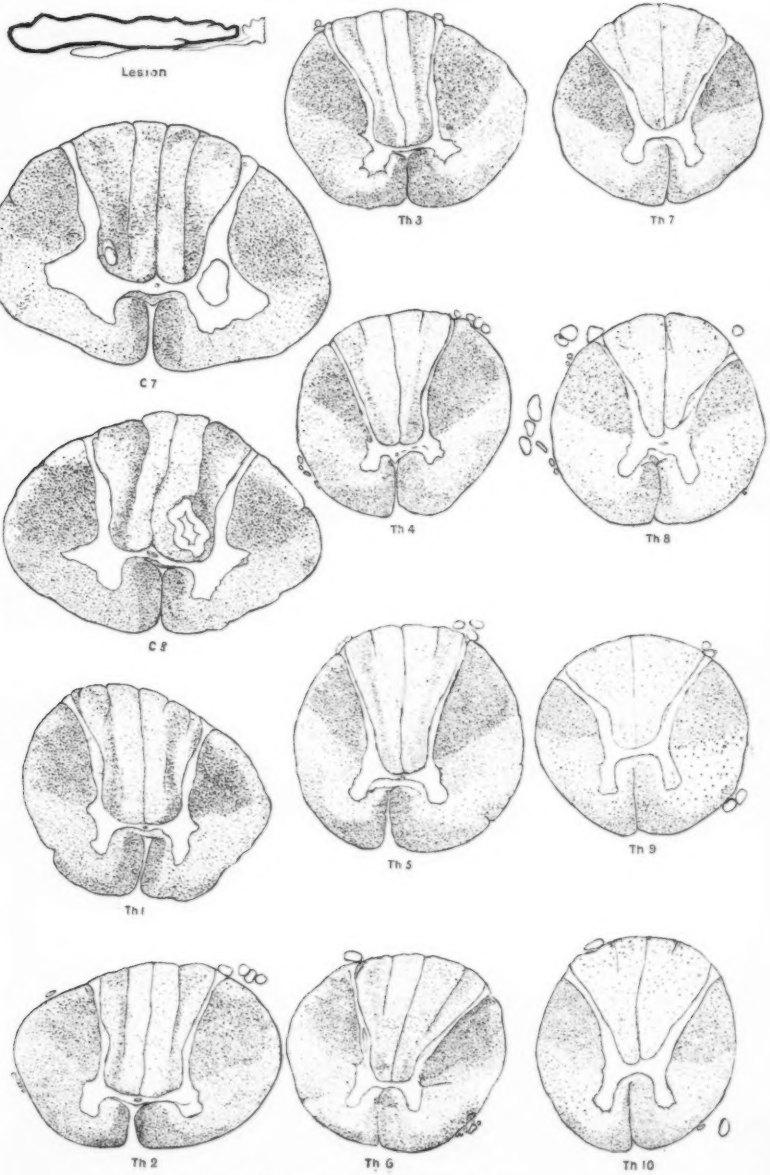
## Ascending Degenerations.




**Ascending degenerations in upper cervical cord.**

# PLATE 5.

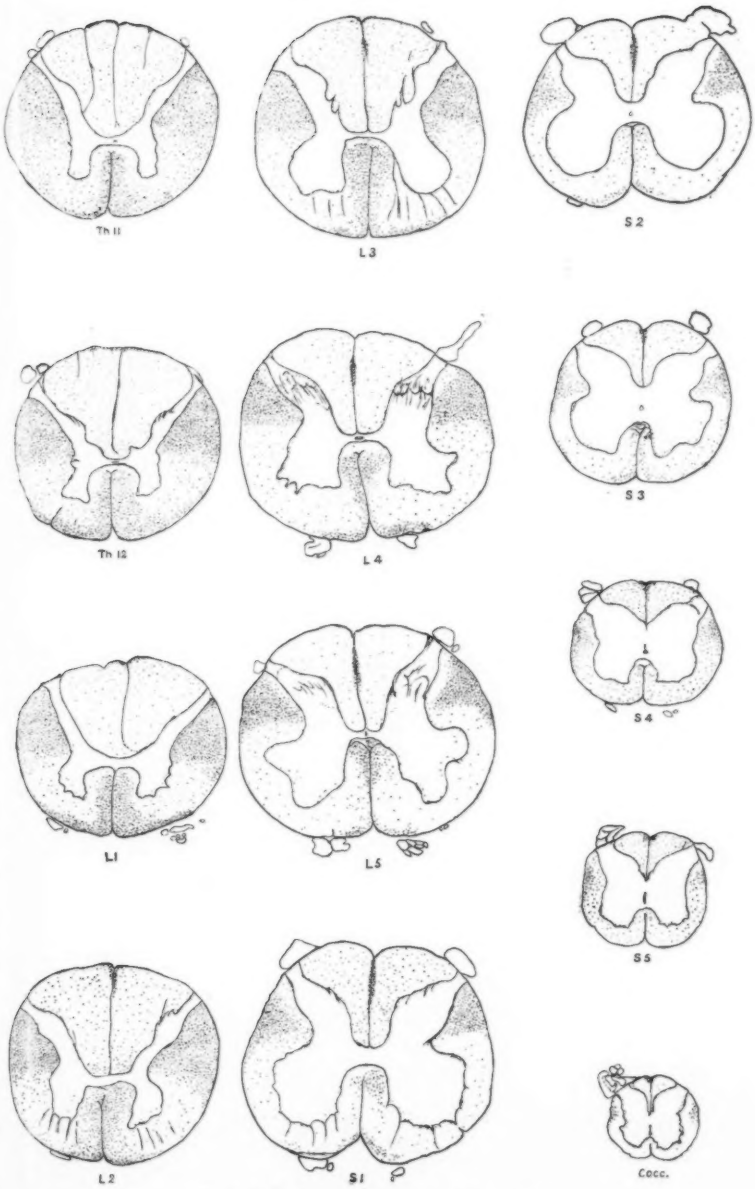
## Descending Degenerations.




From level of lesion down to 10th thoracic segment.
"Tract X" in C. 7 and C. 8 segments.

# PLATE 6.

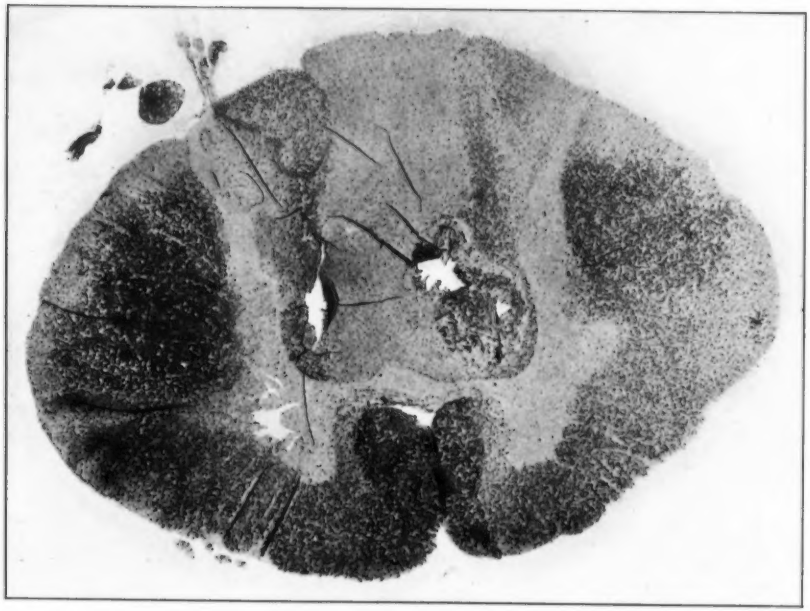
## Descending Degenerations.




From 11th thoracic to coccygeal segment.

PLATE 7.

Schultze's Comma Tract.
V



< Crossed Pyramidal Tract.

< Tract "X."

Photograph of section through lower part of 8th cervical segment.

tract from which it is not sharply marked off, is seen at the level of the 5th cervical segment to be in apposition to the surface of the cord, whilst its anterior end or tail is spread out diffusely and does not cling so closely to the surface. It extends ventrally in amongst the anterior nerve-roots and its precise anterior limit cannot be defined owing to the existence of degenerated fibres in the ventral pyramidal tract (see later). On tracing Gowers' tract upwards through the medulla, it runs ventral to the dorso-lateral cerebellar tract, and when the latter enters the restiform body, Gowers' tract remains at the surface as a triangular mass with its base at the side of the medulla and its apex pointing inwards towards the posterior border of the inferior olive, where it becomes somewhat teased out. In the pons, at the level of the 5th nerve, the tract sinks inwards and lies internal to the trigeminus. It runs ventral to the 7th nerve and dorsal to the fibres of the middle peduncle, and sweeps outwards again to run upwards in the lateral fillet external to the superior cerebellar peduncle. In the lateral fillet its fibres are not scattered diffusely all over, but occupy the central part of that area, leaving a clear undegenerated space both to the outer and inner sides. From the lateral fillet its fibres can be traced to the valve of Vieussens, where the fibres of the tracts of the two sides are seen to intermingle. Sections through the posterior corpora quadrigemina show a few fibres in the region of the lateral fillet, diffusely scattered through the latter. The regions of the anterior corpora quadrigemina and the parts at a higher level were not obtained for examination.

So far as our results go, they are in accordance with those obtained by Hoche,[17] von Sölder,[21] Patrick,[26] and Worotynski,[22] who trace Gowers' tract through the corpus trapezoideum to the region of the corpora quadrigemina. Its further course, whether, as stated by Mott, bending in a loop backwards to stream into the cerebellum, or, as Henneberg[27] maintains, sending a few of its fibres to end in the ventro-posterior part of the lateral nucleus of the optic thalamus, the main mass meantime turning back into the cerebellum, could not be studied in our case.

(3) *Pyramidal tracts, ventral and lateral.*—Although, in a section at the level of the 5th cervical segment, the ventral and lateral pyramidal tracts are sharply mapped out by their relatively scanty degeneration when contrasted with the marked degeneration of the remainder of the antero-lateral columns, yet on close examination they are found not to have escaped entirely. As we trace them to higher levels, distinctly degenerated fibres, although scanty and diffusely scattered, can still be detected throughout the pyramidal tracts in the cord, medulla and pons, *above* the level of the cervical lesion (see plate 3).

Whether this degeneration extends up to the motor cortex it is unfortunately impossible to state, since the structures above the pons are not available for examination. The question as to whether this degeneration is an "ascending" or a "descending" one is for the same reason, impossible of determination, for although on the one hand it might be that it is an "ascending" one, due to the spinal lesion, yet it is also conceivable that at the time of the accident a few of the cortical motor cells might have suffered, producing a descending degeneration in the pyramidal system. At the same time it should be remarked that there was no clinical evidence of such cortical injury. Even within a few hours of the accident, the patient showed neither mental impairment nor weakness of muscles above the level of the lesion.

## Conclusions.

The following are the chief conclusions drawn from the study of this case:—

(1) There is a descending tract,—"Tract X," in the cervical region, situated ventro-external to the crossed pyramidal tract, separated from the latter by a distinct interval at a plane corresponding to the tip of the lateral horn of the gray matter. It does not extend below the level of the 8th cervical segment. It somewhat resembles in shape, but differs in position from the tract described by Helweg and v. Bechterew.

(2) The fibres of the lateral pyramidal tract, after a lesion in the cervical region, degenerate to the most caudal extremity of the cord.

(3) The ventral pyramidal tract extends as a distinct bundle to the 4th sacral segment, below which level its fibres become diffused throughout the anterior columns and are traceable to the most caudal extremity of the cord.

(4) The efferent ventro-lateral tract extends downwards as far as the 4th sacral segment. Below this level its fibres become diffused over the antero-lateral column. Those fibres which lie nearest to the anterior median fissure extend as a distinct tract farther caudally than the outer fibres.

(5) Degenerated fibres occur in the white commissure for three segments below a lesion in the lower cervical region.

(6) Descending degeneration in the posterior columns occurs in the "comma" tract of Schultze as far down as the 9th thoracic segment. Below that level, degeneration continues successively in the "septo-marginal" tract of Bruce and Muir (10th thoracic to 2nd lumbar), in the "oval field" of Flechsig (3rd lumbar to 2nd sacral) and in the "triangle médian" of Gombault and Phillippe (3rd sacral to caudal extremity). No demarcation can be traced between the fibres of the "comma" tract of Schultze and those in the other three descending tracts farther down in the posterior columns. It is therefore probable that they all form one long combined system.

(7) Ascending degeneration of the posterior columns above the level of a cervical lesion does not stop abruptly at the posterior column nuclei. Some degenerated fibres run on both in the internal arcuate and in the postero-external arcuate paths.

(8) The ascending antero-lateral tract of Gowers extends upwards through the lateral fillet through the superior medullary velum (where it mingles with the fibres of the opposite side) to the posterior corpora quadrigemina. In the lateral fillet, the fibres of Gowers' tract occupy the central part of that structure and do not extend to the margins, either externally or internally.

(9) Degeneration also occurs in the pyramidal tracts in

the cord, medulla and pons above the level of the cervical lesion. Whether the degeneration be a true ascending one or not, it is impossible to determine from this case.

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# OBSERVATIONS ON THE MINUTE STRUCTURE OF THE CORTEX OF THE BRAIN AS REVEALED BY THE METHYLENE BLUE AND PEROXIDE OF HYDROGEN METHOD OF STAINING THE TISSUE DIRECT ON ITS REMOVAL FROM THE BODY.

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## I.—Concerning the Technique of the Method.

Since the preliminary notice of this process, which appeared in the Autumn number of Brain, 1900, I have been engaged in making further trials with it, from the results of which it appears as though the reaction is even more capricious and uncertain than I then thought, and that for its success other conditions must be complied with beyond those specifically mentioned in my first account.

A series of trials, closely following those, the results of which I published, on a dozen or more different brains, nearly all resulted in complete failure, no trace of the reaction being obtained except once in the case of a cerebellum, and this was very good.

During this time the weather had been dull, and the bottles containing the tissue to be stained had been placed far from the window of the room they were in.

As nearly all the successes happened during the summer months, it occurred to me that perhaps heat or light had something to do with the matter.

So far although not able altogether to eliminate the effects of heat in aiding the reaction, I think from the trials I have made that at any rate it takes a very subordinate

part; but as regards light this seems to be essential. After many failures, using different proportions of peroxide of hydrogen, different solutions of methylene blue, and keeping the tissue at different temperatures I have obtained a success or modified success in a certain number of pieces which have been kept fully exposed to the light, and perhaps the modified nature of the success is to be ascribed to the season of year, and the extremely dull weather that has been the rule during the time these trials were made.

In November, December and January, during which period these experiments took place, the active properties of light is at its lowest, and very likely as this increases in the summer months the results will be found to get correspondingly better.

The series of trials to show the effect of light were made on pieces of tissue from twenty-four brains; and they were put into a mixture of a 1 per cent. solution of methylene blue—four parts, a 10 per cent. solution of peroxide of hydrogen—one part, and left for nine to eleven days against a window and not interfered with. Of these fourteen turned out more or less successfully, but only five or six were really good, and most of these were pieces of cerebullum.

That very cold weather has a deterrent effect on the process is rendered probable by the fact that during the late cold weather in February and March not a single success was obtained in nearly thirty specimens of different brains, but later on as the weather became warmer, using the same solution and under similar conditions, successes were again the rule.

One other point must be noted—I have never got the reaction in the brains of animals freshly killed or human brains very shortly (a few hours) after death. It seems that a certain stage of decomposition in the tissue is necessary before it takes on the stain in the required way.

As lactic acid is produced during this decomposition I have lately added four to eight drops to a pint of the staining solution, but although some good results have been obtained after this addition, it is yet too early to speak definitely as to the desirability of this addition as a routine practice.

Further trials since the above was written seem to confirm the idea that the addition of lactic acid is desirable. I even add as much as three drops to 40 cc. of the staining mixture (the amount usually employed in individual cases). This addition renders the tissue more brittle—but in cases where pieces of tissue were placed in this strongly acid mixture and others from the same brain in a very faintly acid solution, whilst the former were successful the latter were not, other conditions being the same.

In the previous notice of the method, reference was made to the partial character of the reaction, and it was mentioned that only little patches of the tissue show it, and the first layer and superficial part of the second never stain successfully. To this must be added the fact that in the cerebellum with very few exceptions the reaction occurs at the bottom of a sulcus and usually gets less marked towards the top of the sulcus, and although the granules are deeply stained, yet in this layer there is never any sign of the reaction. No appearance of the processes of the granule, cells, &c.

It is also in the deeper or interior parts of the block of tissue that as as a rule the best sections are got, sometimes indeed when the first few outside sections of a block show scarcely any reaction, those more in the centre will show it well.

In passing I may remark, as it may have some bearing on the question as to the nature of the small darkly-stained structures in the cortex, whether they are of nervous or neuroglial origin, that the latter form of cell in the medullary substance of the cortex are often seen, both in the cerebrum and cerebellum, but they stain of different colour to the nerve-cells and processes. Both the cell body and processes are of a somewhat pale reddish tinge.[1]

In the places where the re-action occurs fully the process probably brings out greater detail of structure than any

[1] Occasionally the neuroglial fibres of the first layer in pathological conditions stain clearly as dark, smooth, wavy, or crenated fibres. A similar appearance is sometimes seen in the cortex cerebelli when the radial or Bergmann's fibres stain as above noted, and appear very similar to the basket fibres.

hitherto known method, for it is quite equal to gold, silver or mercury in picking out the fine ramifications of nerve fibres, but further than these it appears to differentiate between different nerve-cells, so that while the pyramidal system and the Purkinge cells are stained faintly others are very darkly stained. The latter, which are further distinguished by size and shape, would appear as though in ordinary methylene blue staining they are not shown at all or probably only their nucleus is stained, for we see in unsuccessful preparations of cortex stained by the peroxide method that there is no trace of them to be found, whilst in slightly successful pieces one of the first indications of the reaction is the picking out more or less clearly of these cells.

While the opaque character of the impregnation with silver or mercury more or less obscures all detail in and immediately around the cell, the present method, even in the case of the darkly-stained cells, allows fully the interior and surrounding detail to be seen.

And finally, another advantage of the method is that it appears to be permanent, for some of the sections I have now before me have been kept for over two years and show no deterioration.

The foregoing remarks regarding the technique of the method must be taken as representing conclusions only provisionally arrived at, and one reason for publishing these observations in what may be regarded as a premature state is that others may be induced to experiment with the complicated conditions necessary for success in this very elusive process, a process, however, which gives promise of being of considerable service to those engaged in the study of the structure of the nervous system in health and possibly also in disease.

Another reason is that as the specimens I have show clearly the appearances on which my deductions are founded, I think it advisable to publish the results without waiting for further developments in the method; for although as mentioned before, so far the sections appear permanent it is yet possible they may deteriorate in process of time, or get

damaged, and with the uncertainties of the method in view, I may not be able to replace them by others as good.

The following summarises the steps in the process as at present adopted:—

(1) An old-standing 1 per cent. solution of methylene blue (Grubler's pat. b. x), kept exposed to light and air till its *pithy* smell has disappeared. Probably the addition of four to eight drops of lactic acid to the pint is an advantage.

(2) A mixture of four parts of this to one of a 10 per cent. solution of peroxide of hydrogen. The pieces of tissue are placed in this mixture in a fairly capacious bottle, and kept exposed to light, and if very cold weather at a temperature of 25° to 30° C. for eight or nine days.

(3) Twenty-four hours or more in 10 per cent. molybdate of ammonia.

(4) Washed in running water about twelve hours (all day).

(5) The following evening and night in several changes of absolute alcohol.

(6) The next morning through several changes of xylol for two hours.

(7) Two hours in paraffin bath.

Following these instructions, in the summer time under favourable conditions of light and temperature, the successes will probably be in the proportion of nine or ten to one failure; whilst during the winter and dull weather the reverse will be the case—only one success to about nine or ten failures.

In the following pages I propose to consider briefly the structures shown by this method in the cortex of the cerebrum and cerebellum, and to suggest what seems to me to be the most probable inferences to be drawn therefrom. In the description given of the molecular layer of the cerebellum I am quite aware that the main features noticed will be familiar to workers in Golgi's method; but even so, they appear worthy to note, inasmuch as this latter method has, I believe, been chiefly limited in its application to the cerebellum of animals or human embryos,

and therefore, at the least, the results I get are a corroboration of those obtained by Golgi's method; especially as it has been contended that the so-called staining of this latter process is due to impregnation about the nervous structures of precipitated metal in a fine state and not to a true staining of these structures.

Of course the limitation of the stain, in my method, to the molecular and Purkinge cell layers is a serious drawback to its utility in tracing the further course of nerve-fibres.

## II.—Cerebrum.

This method reveals around the pyramidal and giant-cells of the cortex a delicate beaded network (see figs. 1, 2, and 3) loosely enveloping the cell-body and its apex and processes, and extending along the latter as far as it is ever possible to trace them in sections. In some specimens the beaded network can be clearly seen enveloping like an open-work stocking the dendrites of the giant-cells for a distance of 300 $\mu$. The beads on this network stain, as do the fibres, nearly black, and vary considerably in size and shape, some being round, others of irregular contour, and others ring-like. The large irregular beads sometimes appear as if two or more small ones had blended together. The usual size of these beads is about 1 $\mu$, but large ones are met with of 2 or 3 $\mu$ in diameter. Where the branching of the network occurs, the fibres always appear to spring from a bead, and not from intermediate portions of the fibril. The distance apart of the beads varies considerably; over some of the giant-cells, where they are generally large in size, they may be clustered very closely together, but a distance of several $\mu$ usually separates them. Now, this network does not appear as a closed network drawn over the cell; but presents on all sides tags formed by beaded fibres, passing off from it into the surrounding matrix (see figs. 2 and 3), and it is not unfrequently possible to trace some of these fibrils into the stouter fibres, which have all the appearance of being dendrites from neighbouring cells;

also, in like manner, branches can be found which give off fibrils to supply the network of two adjacent pyramidal cells (see fig. 5).

*I wish to emphasise the statement that fibres coming off from different parts of the network can be traced running in different directions in the surrounding matrix, and in some cases can be traced to the thicker branches, evidently proceeding from different cells, because it implies that the cells from the branches of which the network is ultimately formed are in organic continuity one with another by means of this network, and this holds good whether, as some think, the network is an extension of the collaterals of other cells, or whether, as I think, it is an extension of the dendrites of the small dark cells.* This beaded network is apparently a very persistent structure, and is still found in brains which are the seat of extensive pathological changes, *e.g.*, in the brains of general paralysis and dements.

Two varieties of cells are distinguished by this method—pale and dark. A cursory reference was made in my former communication to this fact, and it was pointed out that whereas the cytoplasm of the majority of the cells (pyramidal and giants) stains very lightly others are picked out which stain very darkly.

The cytoplasm of the pyramidal and giant cells stains uniformly and very lightly, so that the apex and dendrites are not prominent features and can only be discovered near the cell body. The nucleus is plump and consists of darkly stained granules closely packed and contained in a definite and darkly stained membrane. The nucleolus as a rule is paler than the nucleus and indistinctly outlined.

It will be seen that this description applies also to pyramidal cells stained by the intra-vitam method.

Amongst the pyramidal cells we meet with instances of dark staining, more especially among the giants, but the infrequency with which these occur in proportion to the numbers which are lightly stained points to a pathological cause for this difference.

And furthermore, one always meets with more dark-stained pyramidal cells in brains which have undergone

obvious pathological changes than in brains from cases of recent insanity.

Although as just stated in the pale-stained pyramidal cells the dendrites are a very insignificant feature and can rarely be traced far, yet in the brains of certain dements of long standing we find many of the pyramidal and giant cells very deeply stained and showing a great wealth of dendrites which are irregular in contour and can be traced for long distances. Now these processes, both apices and dendrites, appear to give off nearly at right angles numerous very fine fibrils.

Even although we grant that this dark coloration of the cell is pathological, this does not alter the significance of the fact in showing the extensive ramifications of the cell branches, for it will scarcely be admitted that a morbid process will have any marked effect in the production of this extensive ramification, or in causing any decided change in its general configuration. We must admit, I think, that the processes thus shown are normally present although only occasionally stained.

One point must be borne in mind, when the cell and its processes are deeply stained the fine investing network is naturally obscured, and I think that quite possibly the irregularity noticed in the dendrites is due to this investing network and that some at least of the fine fibrils mentioned as passing off from these dendrites are in reality fibrils *coming to* them to join the network.

In deeply-stained giant-cells sometimes the axis cylinder can be seen passing off as a darkly-stained, perfectly smoothly outlined fibre, but which, after passing 50 or 60 $\mu$ from the cell, loses its colour and appears as a smooth, very pale strand; and these stout pale strands representing axis cylinders are generally seen running in the lower part of the cortex.

The dark cells of the cerebrum present considerable diversity in shape and size, but the great majority are between 20 and 24 $\mu$ long and of a more or less spindle shape, although not unfrequently one meets with square or pentagonal forms (see figs. 4, 8, 9).

While the cytoplasm and its extensions stain deep blue, the nucleus appears as a homogenous and black mass. The processes of these cells, which are given off all around the body, spring from it at once as comparatively slender branches which can often be traced for 200 $\mu$ or more. They do not branch much as a rule (I am not referring now to the very delicate threads given off all along nearly at right angles to the main stems), and generally begin as shaggy fibres, passing, as they get finer, into moniliform or beaded fibrils.

It is from the dendrites of these cells that I believe I have been able in several instances to trace directly the beaded fibrils of the network about the pyramidal cells.

Apart from the shaggy processes above referred to, sometimes one sees a perfectly smoothly contoured fibre of small calibre passing off from the cell, but in all cases where I have seen this smooth fibre it could only be traced a short distance before passing out of the plane of the section, or perhaps (as with the axis cylinder of the great cells) losing its colour. As very often this smooth fibre is given off from the upper part of the cell and runs towards the surface of the section, it seems probable that some, at any rate, of these dark cells are Martinotti's cells (see fig. 9).

These dark cells are found scattered throughout the cortex from the second layer inclusive down to the medullary substance.

These dark cells are chiefly if not entirely limited to the region of the granule cells in the occipital cortex so far as my observations show. And they are clustered together in amongst the granules in greater number than I have met with them in either the frontal or ascending frontal cortex.

There is never any sign of a beaded network around them or their processes.

Briefly summarised, the following are the main features shown by this method :—

(1) That there are certain cells, the body and dendrites of which stain very lightly and their nucleus dark, granular, and sharply defined, and that the axis cylinder of these cells, when it can be seen, is smooth and of a very pale blue colour.

(2) That a network of fine beaded fibrils loosely invests these cells and their protoplasmic processes, and that beaded fibrils pass from this network at many different points, and that in some cases these can be traced joining to stouter, somewhat shaggy fibres.

(3) That there are certain darkly stained cells, generally small, often pear-shaped or pentagonal, and which give off fine dark-stained processes, which processes can often be followed for very long distances with very little branching.

The finest branches of these cells are beaded or moniliform, and appear very similar to the beaded fibrils of the network.

(4) These dark cells show no signs of any network around them.

Sometimes fibrils can be directly traced from these cells to the network. (This last observation must be separated from the former because before it can be accepted as a fact it will require further corroboration.)

The above, I submit, are four observations that can be verified by any one inspecting my specimens or preparing others by the same method, and from these I would draw the following inferences: First, as to the origin and significance of the beaded network. There are good reasons against the supposition that it is a supporting network of neuroglial fibres, for in the first place the neuroglial elements do not usually stain by this method, and when they do they stain of a rather pale reddish tint and their fibrils are not so distinct or so dark,[1] and in the second place Golgi's method shows in the ending of certain peripheral sensory nerve fibrils just such a beaded appearance as is seen in the network, and no process that I know of has ever shown anything like a beaded appearance of the neuroglial fibres.

Excluding then the neuroglia I think we may fairly certainly assume that the network is formed by the processes of nerve-cells.

As to their being the extension of the collaterals of axis cylinders we must bear in mind that the axis cylinders, as seen in the lower part of the cortex by this method, appear

[1] *See* foot-note, page 240, for exception to this statement.

as very pale blue and smoothly contoured fibres, and collaterals are not certainly stained at all. By this I mean I have never seen a dark collateral given off from one of the pale axis cylinders, although of course it is possible that the ultimate terminations of the collaterals may stain differently from the same fibre at its origin from the axis cylinder.

As to its being an extension from the dendrites of the pyramidal cells, these usually are very pale and soon disappear from the plane of the section, and although they sometimes colour deeply and can be traced for long distances, it is not only in these cases, as we should expect if they gave origin to the network that this latter shows, but even when the pyramids and processes do not colour at all.

Now in favour of the assumption that the network is formed by extension of the dark cells we have the fact that the processes of these cells always stain deeply and of the same colour as the network, and in all physical characters, they appear similar to the fibrils of the network.

And finally, I believe that in several cases I have been able to trace a fine beaded fibril coming from a dark cell directly to a network, so that the balance of evidence seems to be in favour of this network being as it were an extension of the ultimate fibrils proceeding from the small dark cells.

If we accept the above interpretation it must lead to considerable alteration in our conception of the arrangement of the nervous elements in the cortex of the brain, *for it implies that there are at least two systems of cells present, the pale or pyramidal variety, and the small darkly-stained variety, and these latter branch in all directions and their dendrites ramify and ultimately form a network about the former, and the whole system of dark cells is in absolute continuity one with another through the medium of the network.*

### III.—Cerebellum.

Figs. 9 and 10 give a general idea of the appearance of the cerebellum as shown by this method.

In fig. 9 chiefly the small cortical cells (Shaffer's cells)

are shown, and although numerous delicate fibrils are seen given off from them and interlacing in all directions, yet the photograph gives but a very poor idea of the wealth of fibrils actually shown in the sections, and to see which it is necessary to shift the focus.

In fig. 10, more highly magnified (×400) the lower half of the cortex only is shown, and the dark cells seen are chiefly basket cells. In the lower border of the figure there is a Purkinge cell enveloped in its sheath of basket fibres.

The Purkinge cells, as a rule, stain lightly, and show no trace of chromophilic material; the nucleus is dark and granular, and with a sharply defined border; the nucleolus varies, but is often pale and indistinct.

Variations in this way of staining have been pretty frequently met with, but as I am dealing with pathological material, it seems probable that these variations are due to morbid conditions, and I have taken as normal the form most frequently met with in the young and in recent cases of insanity, and which is most nearly allied to the staining obtained by the *intra-vitam* method. In the majority of cases the branches of the Purkinge cells either do not stain or else stain very lightly, but occasionally these also are dark, and indeed sometimes darkly coloured branches are seen originating from a cell with pale body. Of course it is only when they are darkly stained that we get a view of the great wealth of branches given off and showing then as a rule, little lateral projections or thorns (figs. 12, 13, 14).

Even if the supposition is correct that a dark colour implies a pathological condition of the cell and processes, this does not necessarily mean that thorns are a pathological feature, but that under normal conditions they do not take on the stain.

The ramifications of the Purkinge cells extend quite up to the surface of the layer, and the main stems do not bear thorns, only the terminal twigs.

These thorns take the shape of a short delicate lateral fibril ending in a knob. I find that they are of common occurrence when the branches from which they spring stain deeply, and when met with they occur all along the processes,

and not one here and there, although Obersteiner says ("Anatomy of Central Nervous Organs" translated by Hill, edition 1900, p. 405), speaking of Golgi's method:—"In perfectly successful preparations of the brains of adults no such excrescences appear, only a granule here and there is seen attached to the processes of an isolated cell."

In the case of a man 68 years old, suffering from melancholia, although there was very manifest atrophy of the branching fibres of the Purkinge cells, yet the lateral projections with knobbed ends were very distinctly shown (fig. 12). The atrophy referred to is not a necessary accompaniment of age, as in another man of 68, the branches were as plump and broad as usual.

In the lower half of the molecular layer in sagittal sections (across the direction of the foliæ) are seen a number of stout (1 to 1·5 $\mu$), smoothly contoured, wavy or crinkled fibres, which run for the most part parallel one to another and to the surface of the layer and stain deeply. Not unfrequently one of these fibres bends back abruptly and runs in an opposite direction.

These fibres originate (in part at least) from small (12 to 15 $\mu$), oval or pear-shaped cells lying in amongst them and usually with their long diameter in the direction of the fibres. These cells stain deeply, and for this reason it is often difficult to distinguish the nucleus from the cell body. Besides the stout, smooth, parallel fibre, which is said to be the axis cylinder and which passes generally from one end of the cell (and sometimes apparently one from each end), other branches are given off. These generally divide near the cell into very delicate fibrils, which may appear to end shortly, as for example when they run in the direction of the granular layer, or else as when they spring from the upper side, may often be followed for very long distances without further branching. Some of these long, fine branches running upwards can be traced to within a few microns of the surface of the layer and there double back and run down in an opposite direction, traversing in their downward course considerably more than half the width of the layer, so that altogether these delicate processes

can sometimes be distinctly traced for the surprising distance of over 400 $\mu$.

The parallel fibres give off as they run along, branches at right angles, which, for the most part, run towards the granular layer; sometimes a branch given off from the upper aspect of the fibre (fig. 16) bends down and runs inwards to form the basket work around the Purkinge cell.

Often one is able to directly trace the passage of a parallel fibre or its branch into the basket work and this structure loosely envelopes the cell and the fibres of which it is formed meet together at some little distance below the invested cell.

As a rule the fibres going to form these baskets widen out and appear flat and tape-like in their passage over the cell (fig. 15).

A number of branches coming from different parallel fibres often meet together in a dense mass as they reach the cell (fig. 17).

In the great majority of instances the fibres of the basket work run over the cell in the same direction as its long diameter, but occasionally transverse strands are seen (fig. 16).

Sometimes instead of a right angle branch of parallel fibre running to form the basket work the fibre itself ends by turning down for this purpose (fig. 17).

The flat tape-like looking fibres often attain a width of 2 or 3 $\mu$, and generally speaking, the whole structure of the basket work is made up of coarse fibres which very loosely envelope the cell. I particularly mention this as Obersteiner (p. 406) speaks of these fibres as " brushes of extremely fine fibres which fix on or closely encircle the aforesaid (Purkinge) cells," although the translator of this work (Dr. Hill) correctly figures the structure in his work on the Golgi method, and it is correctly figured in the latest edition of " Quain's Anatomy."

The basket fibres often envelope the branches of the Purkinge cells some distance from the cell body before passing down to form the basket work proper.

Apart from the above-described system of stout enveloping

fibres, there is, both around the Purkinge cell and its main branches, a network of delicate beaded fibrils, very similar in appearance to that seen about the pyramidal cells; whilst, however, it is only occasionally that these delicate fibrils can be detected over the body of the cell, they are comparatively frequently met with over the branches.

Beaded fibrils can also be seen coursing about in different directions in the surrounding matrix, but generally only in the region of the parallel fibres. I have not been able to determine where these beaded fibrils come from; sometimes they seem to be delicate fibres passing off from a basket fibre. Probably, I think, some at least originate from the small cortical cells higher up in the layer, for these generally present a decided but slightly beaded aspect.

W. Aldren Turner and W. Hunter ("On a Form of Nerve Terminations in the Central Nervous System demonstrated by Methylene Blue," BRAIN, vol. xxii., pp. 123-134) failed by the intra-vitam method to detect this delicate lattice work in the cerebellum; and, as by this method, the basket work is also not shown, they argue that this latter is not a nerve arrangement, but neuroglial. I think, however, the fact that it is stained by the present method in such a distinct way and that it can be traced as arising from the darkly stained cells lying in this region will not permit us to accept this view; especially, as the neuroglial elements do not usually stain, and, when they do, they take on a quite distinct colour to that assumed by the nervous elements.

The remaining part of the molecular layer (that is, the outer half), beyond the expansion of the Purkinge cells already alluded to, is occupied by a number of extremely small (9 to 11 $\mu$) very dark cells of different shapes (triangular, square, oval, pear-shaped, &c.), which give off numerous delicate branches on all sides, forming an intricate network in this region. These branches are almost always moniliform or beaded, but the beads are generally only very slight swellings on the fibre, and not nearly so clearly defined as those seen in the cerebrum. The cells are most thickly congregated in the middle third of the layer, but they are met with lying quite close to the surface and also down

among the basket fibres near the granular layer, and it is often very difficult or even impossible in this region to distinguish them from the basket cells ; the main points by which we can most certainly differentiate them being the rather larger size and more regular disposition of the basket cells, and the fact that it is these cells only that give off stout smooth fibres running in a parallel direction.

Fig. 10 gives some idea of the relative number and variety in shape of these small cells. Their processes can often be followed for long distances, but their ultimate destination cannot with any certainty be made out, although unquestionably they must be brought into very close relationship with the thorny branches of the Purkinge cells amongst which they lie.

Briefly summarised, the results arrived at from the examination of the cerebellum by this method are as follows :—

(1) It has a selective influence in regard to the staining of the different nerve-cells, some (the Purkinge cells) being very lightly stained, and others (small cells) very deeply stained.

(2) The dark cells can be subdivided into those which certainly envelope the body of the Purkinge cells by their branches and those which, although one is not able with certainty to trace their branches to their destination, there are grounds for supposing invest the branches of the Purkinge cells with a fine beaded network.

In conclusion, I will refer briefly to some inferences that I have been tempted to draw from the foregoing observations.

It seems only reasonable to suppose that the difference in colour, size and shape, &c., of the cells we have met with both in the cerebrum and cerebellum is associated with a difference in their function, and as we have considerable evidence in favour of the pyramidal cells being concerned with efferent impulses. I would suggest that the others—the small dark variety—are concerned with afferent impulses, that in a sense they serve as collectors of ingoing currents

which, after passage through them, are distributed to the pale cells with which they are in association.

Although there is considerable difference in the size of the dark cells of the two regions of the brain examined, yet, as they both react similarly to the methylene blue I consider that this, taken along with certain morphological similarities before referred to, will be some justification in associating them together for the purposes of comparison. Now we find that the proportion of dark to pale cells is very different in the cerebrum and cerebellum. In the former they are few in number relatively to the pyramidal cells, in the latter they far outnumber the relatively few Purkinge cells.

Thus we appear to have in the cerebrum a condition the reverse of that found in the cerebellum. In the former there are numerous efferent cells in relation with comparatively few afferent elements, in the latter few efferent in relation with many afferent.

The interpretation that I have given to these facts harmonises with Spencer's theory that the cerebellum is the great organ for co-ordinations in space, while the cerebrum is the organ for co-ordinations in sequence.

## DESCRIPTION OF FIGURES.

### Fig. 1.

Outline traced from a photograph shows the beaded network over a giant-cell. A beaded fibril is seen passing from (? to) the cell from the upper part of the figure, another from the right-hand side. The size and shape of the beads vary; they are generally about 1 $\mu$ in diameter, some 2 or even 3 $\mu$. Their distance apart also varies from 1·5 to 8 $\mu$. The nucleus of the cell is shown in the lower part of the figure ($\times$ 700).

### Fig. 2.

Pyramidal cell with dense network of beaded fibrils encompassing it. Fibrils are seen passing off from the network in all directions. Although the nucleus of the cell is shown, yet in the specimen, when it was in focus, the network over the near surface of the cell was thrown completely out of the field of vision ($\times$ 600).

### Fig. 3.

Outline, traced from a photograph, shows the network extending along the branches of the pyramidal cell. Coarse fibres can be seen at *a* and *b*, from which delicate fibrils proceed to join the network ($\times$ 700).

FIG. 4.

Traced from a photograph, shows a small dark cell, with thin, slightly varicose processes given off from it (× 400).

FIG. 5.

Shows a dark, stout fibre, dividing and giving off from each division fine beaded fibrils to two pyramidal cells. A stout, dark fibre runs up to the left side of the upper pyramidal cell, and apparently also helps to form the investing network (× 600).

FIG. 6.

Also shows a stout fibre dividing and giving off one fine branch to the network about the pale cell shown, while the other passes upwards, probably on its way to another network. This fibril also shows beads on it (× 600).

FIG. 7.

A pale cell encompassed by stout fibres, from which fine beaded fibrils are given off to pass over the cell (× 600).

FIG. 8.

A small, dark, pyriform cell, giving off only a few branches from either end; the lower ones appear varicose and can be followed for a long distance without further branching (× 600).

FIG. 9.

A dark cell with ascending axis cylinder (*a-c*) which gradually gets paler in colour as it passes upwards. Note its smooth contour. From a stout process a fine fibril (*x*) passes off, along which are little irregular swellings, closely resembling the beaded fibrils of a network. The figure is traced from the photograph which was reproduced in my article in the autumn number of BRAIN (× 600).

FIG. 10.

Molecular layer of cerebellum with small cortical and basket cells (× 300).

FIG. 11.

Basket cells and fibres with a Purkinge cell invested by the latter (× 400).

FIG. 12.

Darkly-stained Purkinge cell branch with lateral processes showing thorns. Note the atrophy of the branches (× 600). From a man aged 68 years.

FIG. 13.

Darkly stained Purkinge cell branches with thorns, also a small cortical cell whose branches are shown intermingled with the thorny processes. From a man aged 41 years. Note the stout character of the branches compared with those in the previous figure (× 600).

FIG. 14.

From the same as the last, showing thorns (× 600).

FIG. 15.

Basket fibres spreading out over a Purkinge cell into flat, broad, tape-like strands. Some seem to subdivide longitudinally (× 600).

FIG. 16.

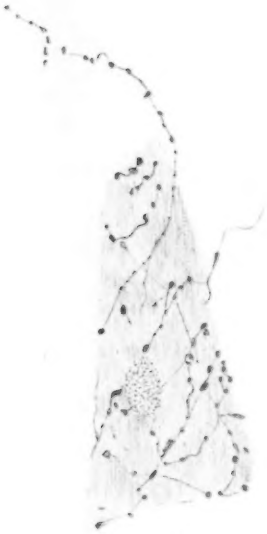
A basket fibre, shown in upper part of the figure, which gives off from its upper side a branch which bends down and goes to help form a basket arrangement around the Purkinge-cell shown in the lower part of the figure. Note the transverse strands and the basket fibres meeting below the Purkinge cell some little distance (× 600).

FIG. 17.

A basket fibre is seen to terminate by bending down to assist in forming the basket work around the Purkinge cell; other fibres are seen coming from other directions and meeting together in a dense cluster to one side of the Purkinge cell, which shows the almost colourless cytoplasm and dark nucleus referred to in the text (× 600).

FIG. 18.

Shows fine beaded fibrils similar to those seen in the cerebrum. Some of these can be seen passing over the Purkinge cell which is just indicated by its slightly darker colouring above the granules (× 600).



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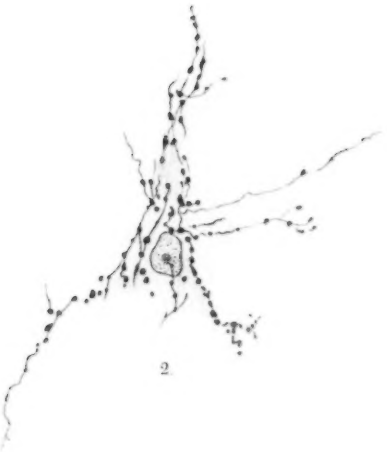

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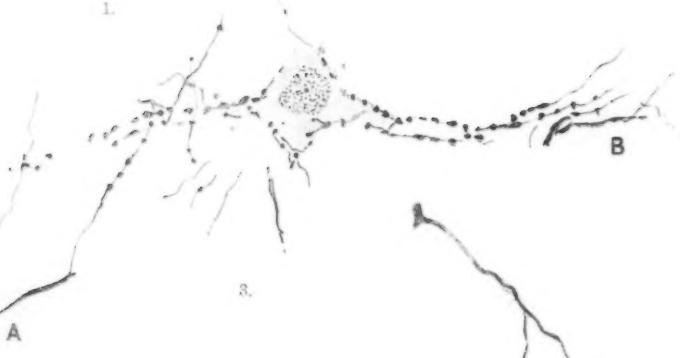


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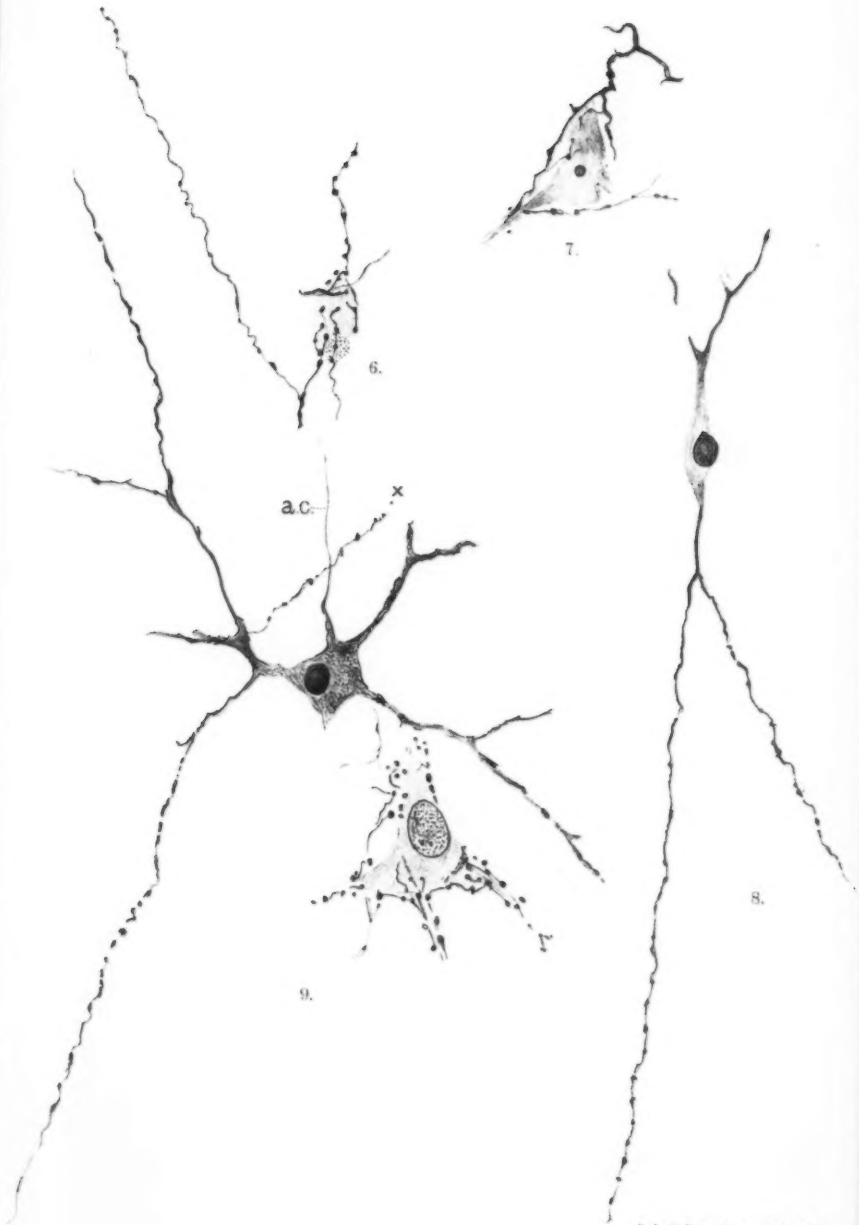


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FIG. 10.

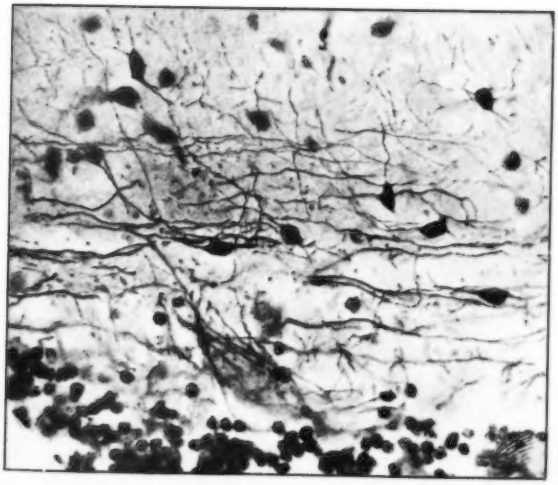

FIG. 11.

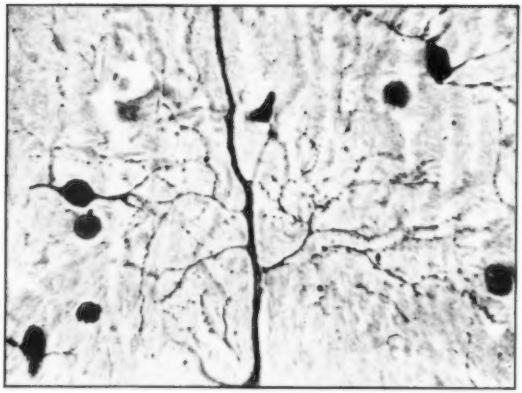

FIG. 12.

FIG. 13.

FIG. 14.

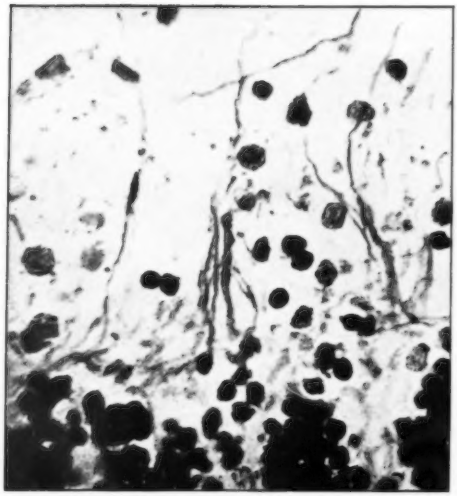

FIG. 15.

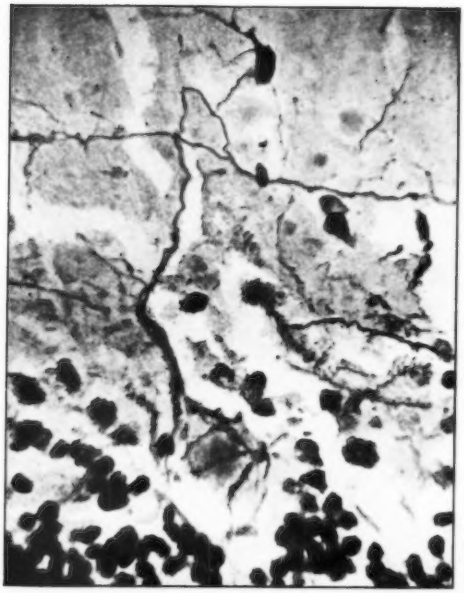

FIG. 16.

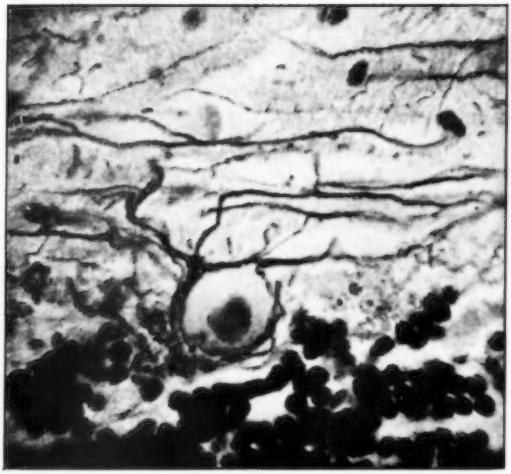

FIG. 17.

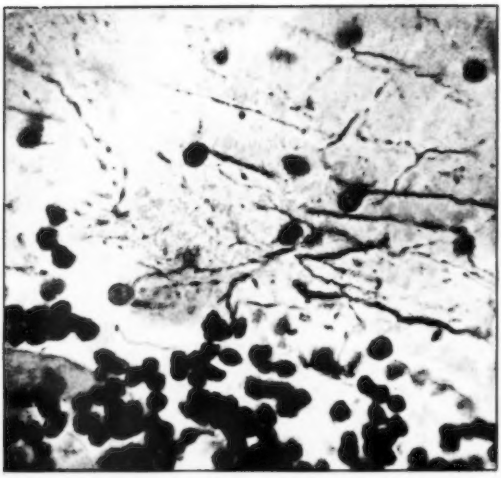

FIG. 18.

# A CASE OF FAMILY PERIODIC PARALYSIS WITH A CRITICAL DIGEST OF THE LITERATURE.

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*Senior House Physician to the National Hospital, Queen Square.*

*Together with a Report, and Digest of the Literature, on the Pathological Examination of the Excreta.*

BY FRANCIS W. GOODBODY, M.D.DUB., M.R.C.P.

*Assistant Professor of Pathological Chemistry, University College, London.*

THE subject matter of this paper has been divided up as follows:—(1) A description of a case of family periodic paralysis which has been under observation in the wards of the National Hospital, together with a report of the pathological examination of the urine and fæces by Dr. Goodbody, of University College, London. (2) A critical digest of the previous literature of the subject; the part of this relating to the pathological examination of the excreta being written by Dr. Goodbody. (3) A full bibliography. The last two parts have been carried out in some detail, because no case has so far been recorded in this country, and no English paper has hitherto appeared on the subject. The records have as far as possible been carefully examined, with the result that certain cases, such as those of Cavaré, Romberg, Gibney, Bernhardt, and Burr, which have previously been included as examples of this disease, but which appear to differ from it in essential features, have been excluded from the bibliography. References to these cases may be found in an excellent paper by Dr. E. W. Taylor in the *Journal of Nervous and Mental Diseases*, New York, for September and October, 1898, to which I am indebted for all the earlier references.

I take this opportunity of expressing my thanks to Dr. Howard H. Tooth, under whose care the patient was admitted to the hospital, for permission to publish this case, and also to other members of the honorary medical staff for kind assistance and advice.

My thanks are also due to Dr. J. K. Mitchell, of Philadelphia, and Dr. J. J. Putnam, of Boston, for sending me reprints of their papers on the subject, and to the former for kind suggestions as to lines of investigation and treatment.

T. L., aged 16, was admitted into the National Hospital on October 12, 1900, complaining of attacks of loss of power for about two years.

*Family and personal history.*—There is absolutely no history of any similar trouble nor of any neuropathic tendency in his family so far as can be discovered. Patient's mother died shortly after the onset of the lad's attacks from morbus cordis, the result of acute rheumatism; his father is a temperate man, but is said also to have heart disease, though he has not had rheumatism. Two sisters are living, strong and healthy; a third died of scarlet fever and diphtheria. Patient was the third child in a family of four, and was quite healthy as an infant, but somewhat backward in walking, not doing so properly until 5 years of age. He is said to have had smallpox as a child, but this seems doubtful, as he bears no scars, and has four good vaccination marks, which were made when he was a baby. At the age of 8 years he had a sudden attack of "cramps" in the legs when out walking with his mother, but nothing further is known of this incident. Whilst at school he tried to learn to swim, and liked the water, but had to give it up because he invariably got cramp in the legs. Apart from the above incidents he has always been very healthy. His habits tend rather to an out-door life, and he is very fond of exercise, but he did fairly well at school, passing the sixth standard at the age of 13. He has always been of a very excitable temperament, and is at times inclined to be violent; his sister asserts that an attack of paralysis always follows one of these outbursts of wild excitement, although the latter are by no means frequent precursors of the attacks. He worked for twelve months after leaving school at a lead-pencil factory, but since the onset of his present illness has had to give up regular work, and has acted as an errand boy. He has lived in fairly comfortable circumstances all his life in Battersea.

*History of illness.*—The first attack of paralysis occurred about two years ago at the age of 14, the second four to six weeks later, and since then attacks have followed at somewhat irregular and gradually decreasing intervals until now they occur about once a week, although a few weeks ago he had as many as three in five days. The onset has always taken place at night, without any known cause or warning, and he is absolutely certain that he is not more liable to an attack after a severe day's exercise than at other times. He accepts the attacks philosophically, his only trouble being that they prevent him from getting permanent employment. The attacks are all very much alike in character, differing only in severity and duration; he never loses consciousness, has never been unable to talk, and suffers only from the discomfort of lying for a long time in one position. On three separate occasions, however, he has had alarming difficulty in breathing, and on the last of these he also had great difficulty in swallowing. During an attack he does not feel any desire for food, but will sometimes drink freely or eat fruit; he is unable to pass urine, but does not feel any desire to do so, and his bowels are never opened until after the attack, even if it lasts for two days. During the first twelve months of his illness he vomited several times soon after the onset of an attack, but this has not occurred lately, though he often feels some nausea.

*On admission* to the hospital on October 12, 1900, he presented a rather feeble appearance, with very little subcutaneous fat and muscles somewhat poorly developed. Mentally he is bright, cheerful and intelligent, and a fair witness. On physical examination, the only abnormalities noted were that the right pupil was a little larger than the left, both reacting normally, and that on lateral deviation of the eyes, there was some irregular nystagmoid jerking, more marked towards the right than the left. Muscular power was everywhere proportional to development, and sensation was normal; all deep reflexes were present, normal and equal on the two sides; abdominal, cremasteric, and plantar skin reflexes also normal, the last of flexor type.

The electrical reactions of muscles were examined on several occasions in the intervals between the attacks, and found to be absolutely normal in every respect.

### *Description of the Attacks.*

Many have been observed whilst in the hospital, but they are all so much alike that it is unnecessary to describe more than

one; the differences merely depend upon the severity and duration of the paralysis. This attack is chosen because it was observed practically from the onset, which took place in the afternoon, patient having been kept in bed for purposes of observation. He had been feeling perfectly well, and, as usual, had no warning whatsoever; he was lying talking to some friends about 3 p.m. when he noticed a "dull aching" about his knees, and found, on moving them, that his legs were weak; the aching was at once relieved by change of position. He also found, on trying to sit up, that he had great difficulty in doing so. His hands and arms were at this time quite strong.

At 4 p.m. The weakness in the legs had very considerably increased, but he could still draw them up in bed, while extension of hips and knees was distinctly better; he could not sit up in bed without assistance. The arms were distinctly weak in the proximal joints, but the change was not nearly so marked as in the legs.

At 4.30 p.m. The legs much in the same condition, but grasp as tested with dynamometer was distinctly less.

At 5.30 p.m. *Upper extremities.* All movements present, with the exception of flexion of the elbow on the right side, but all are feeble. The best movements are those of the fingers and wrists, the left a little stronger than the right. *Lower extremities.* Flexion of hip and knee and adduction of the thighs are now impossible; all other movements are still present, but are very feeble, the best of all being those of the toes. *Neck* muscles are also weak, although the head can be still raised off the pillow, but not against the slightest resistance, while extension of the neck is more powerfully performed. *Trunk* muscles can all be voluntarily contracted, but all are feeble.

The muscles supplied by cranial nerves are quite normal.

*Electrical reactions.*—No reaction to either faradism or galvanism could be obtained in the hamstrings or abductors of the thighs, nor in the right biceps humeri. The quadriceps femoris reacts to both currents, but less readily than normal; the contraction shows no qualitative or polar change. Currents of varying degree, proportional to the amount of voluntary power are required in other muscles. Prolonged tetanisation of the flexors of the fingers of the left hand with a faradic current was maintained, but no diminution of reaction was observed, such as is seen in myasthenia gravis, nor did the subsequent increase in paralysis in the muscles so treated show any difference from that of the opposite side.

Mentally he is perfectly natural, talks normally, and complains of nothing except the discomfort of being unable to change his position.

No change in objective sensibility to any form of stimulus could be detected.

At 7 p.m. he managed to eat a little food, but was unable to feed himself.

At 7.30 p.m. He is quite unable to move the head or shoulders; on sitting him up he simply doubles up and his head falls either forward or backward without his being able to control it in the least. Respiration is almost entirely diaphragmatic; coughing is almost impossible as the abdominal muscles only just contract in the attempt and only the very feeblest movement is perceptible in the latissimus dorsi on either side. All arm movements are very small, flexion of the elbow and extension of the wrist being quite absent on the right, but just present on the left side where extension of elbow and flexion of wrist are quite absent. The fingers on both sides can still be flexed, extended, adducted or abducted though with small power, and the grasp is practically nil. In the lower extremities slight extension and ext. rotation of hips is still possible and the quadriceps can just support the weight of the lower leg. Feeble movements of ankles and toes are present.

*Reflexes.*—Knee-jerks are present but only a very feeble contraction is obtained, though it is noticeable that this is very ready and is not reinforceable. All other deep reflexes are unobtainable. Abdominal and cremasteric skin reflexes absent. Plantars still ready but the movement of the toes is small and flexor in type.

The muscles supplied by the cranial nerves are still normal.

No change mentally or in sensation. Pulse good volume and tension, quite regular. Patient had not passed urine since morning, but there was no obvious distension of the bladder and he had no desire to micturate, but after severe effort he succeeded in passing nine ounces, and about one minute later, after further straining, he passed one ounce more.

9.20 p.m. Sleeping quietly till now. He is bathed in perspiration from head to foot (this was not so ten minutes ago). The face and skin generally is flushed and feels hot to the hand. Temperature 98° in the mouth. Pulse 96 regular, tension low. Respiration 18 regular and easy but purely diaphragmatic. He cannot take a deep breath and cannot cough. In the upper extremities the only movement now possible is a very slight one

in the index finger on either side. The right leg is completely paralysed, but in the left a slight contraction can be made in the quadriceps not sufficient to move the leg, while a very faint contraction in the vastus internus can be produced by tapping the patellar tendon. On the left side also he can just move the big toe and here also a faint plantar reflex (flexor) can be obtained. No other reflexes obtained. Cranial nerve supply normal. Sensation normal.

10 p.m. Sweating has ceased, but the skin is still flushed. Left leg now quite paralysed with the exception of slight movement of big toe with faint plantar reflex still present, knee-jerk quite absent.

11.30 p.m. Some improvement in arms; can now flex fingers and wrists slightly and also pronate and supinate faintly; there is also a very feeble contraction in left triceps humeri with faint triceps-jerk. Right leg completely paralysed with absent reflexes; slight power in left quadriceps femoris and big toe with very faint knee-jerk and plantar reflex.

Coughing and deep breathing are impossible.

The paralysed muscles, although the palsy is of the flaccid type, do not show any degree of hypotonicity and feel firm and solid to the touch; none of them contract to direct percussion.

He now shows for the first time some partial bilateral ptosis, the upper lids cannot be raised above the upper edge of the pupil. The right pupil is markedly larger than the left and has certainly dilated; both however react normally to light and in accommodation. Ocular movements are good in all directions, but still show the nystagmoid jerkings noticed on admission. Facial muscles, masseters, palate and tongue move normally. Swallowing and speech normal.

12.45 a.m. Arms are steadily improving and the biceps and triceps on both sides contract feebly, while their tendon-jerks have returned. Shoulder girdle muscles and those of extraordinary inspiration are still paralysed. Slight movement of toes on right side now present, with return of right plantar reflex (flexor), otherwise legs much as before. The ptosis has very nearly disappeared.

2 a.m. Slight further improvement. Biceps, triceps and supinator-jerks present on both sides. Right knee-jerk absent; left faint. Achilles-jerks: right faint, left absent. Ptosis quite gone. Patient now sweating profusely and skin much flushed and feels hot to the hand although the temperature in the mouth is only 97° F.

3.15 a.m. Some power now in all muscles, best in periphery of all limbs. All reflexes are present, but still feeble.

4.30 a.m. Much improved; he can now move all limbs and head, but not yet able to sit up. Feels well but rather stiff and sore, as if he had done some hard exercise.

10.30 a.m. Power now everywhere good, though still some feeling of stiffness.

The above represents a moderately severe attack, and may be taken as a type. All the severe attacks have come on while the patient has been in bed, and vary in duration from five to twenty-eight hours, generally lasting about twelve to sixteen hours. He however describes one attack that lasted more than two days and nights. During the daytime he has on several occasions complained of stiffness and weakness of the knees and sometimes also of the hands, and on examination his gait is distinctly paretic and his arms weaker than normal, but these have invariably passed off in the course of an hour or so, whether he has taken exercise or has rested. On two occasions while in hospital, when recovering from an attack, which had lasted seven or eight hours, he has relapsed before recovery was complete, into a more severe degree of paralysis than before, the relapse running the usual course and lasting about twelve hours.

*Order of involvement of muscles during an attack.*—This is not by any means constant as regards individual muscles, but certain rough generalisations can be made. The weakness has always appeared first in the lower extremities, and very soon affects lower trunk muscles; it next spreads to upper arm and trunk, involving the neck about the same time. As a rough rule it may be stated that the more proximal limb muscles are the first to be affected, the muscles of the digits being always the last to become completely paralysed. The muscles which have, in most attacks, been the earliest to lose power completely are the hamstring and adductors of the thighs, the quadriceps being affected much later. But this is not constant; in one attack the arms became completely paralysed, including even the fingers, when he was still able to move the legs, although on this occasion, too, the weakness had begun in the legs quite as early if not earlier than in the arms. It has not been possible from the order of spread to attribute

the affection to a progressive involvement of spinal anterior cornual cells. The only cranial nerve muscles that have been affected whilst in hospital are the levatores palpebræ and the right iris oculi. These have been affected on each occasion only during the height of the paralysis.

The intercostals and extraordinary muscles of inspiration are affected early and become completely paralysed; the diaphragm, however, continues to act, although I am inclined to think that it has been to some extent weakened in some of the most severe attacks, because the power of taking a deep breath, and even of altering his shallow breathing in depth at all is entirely lost.

*The order of recovery* is for all practical purposes exactly the reverse of that in which they were affected, that is to say the last muscles to lose power are the first to regain it.

On several occasions marked changes have been observed in the condition of the *heart*. The area of superficial cardiac dulness becomes markedly increased, and diffuse pulsation over the præcordial area, including the second and third spaces to the left of the sternum. The first sound becomes soft and not clear, but I have never heard a definite murmur either at the apex or base; the second sound at the left base is accentuated and reduplicated, while the first aortic sound is feeble. The pulse becomes soft but fairly full and distinctly intermittent. On one occasion breathing was seriously affected and mucous rattling was audible in the larger tubes.

Repeated *electrical examinations* reveal the following facts:—In the intervals between the attacks the muscles all react normally. During an attack there is a gradual reduction of excitability both to faradism and galvanism *pari passu* with the loss of voluntary power, until with complete palsy there is complete loss of excitability to both currents. With the reduction there has never been any change either in quality of contraction, nor has there been any polar change to galvanic stimulation. As voluntary power recovers there is a gradual return of excitability to both currents.

The facial muscles have always reacted normally when

stimulated through the nerve or directly even at the height of an attack.

*Excitability of muscles to percussion* which, during the intervals is normal, disappears at the height of paralysis.

The *reflexes* disappear *pari passu* with the loss of power. It is, however, noteworthy that both with tendon-jerks and skin reflexes, although the amount of contraction produced by the stimulus diminishes with the loss of voluntary power, yet the reflex is still as readily obtained as before, and with only the same stimulus, so that so long as there is the least power of contraction in the muscles a ready even if slight reflex can be obtained ; moreover it can be elicited with the smallest return of voluntary power. Another point of interest is that the contractions cannot be increased by reinforcement.

The *temperature* during an attack has been several times taken at short intervals and has been found to fall slowly to 96° or 97° F., but exactly the same fall occurs quite regularly when taken during a night in which the patient is not having an attack. If the temperature is watched during an attack coming on in the day time no fall in temperature is observed. No rise has been noticed at any time.

### *Relation of Attacks to Muscular Exercise.*

Much stress has been laid by some authors upon the excitation of attacks by severe muscular exercise, but both from the history as given by the patient and from observations while in hospital, this has certainly not been the case in T. L. When first admitted he was kept completely at rest in bed for six days, during which time he had two severe attacks, lasting fourteen and sixteen hours respectively, and also two slighter ones, each lasting five or six hours. He then objected so strongly to being kept in bed that he was allowed to get up and take a moderate amount of exercise, working about the ward and occasionally going for a walk. During the next six days he had only two attacks—one severe, the other slight. In the next ten days he had, however, six attacks, two of them severe and four

moderately so. At the end of that time he used a Whiteley's exerciser twice a day, as well as doing the same work as before. The attacks then diminished to about one per week on an average, sometimes more, sometimes less. At a later period, when he had been having attacks about once a week, he was again kept in bed for a week, and during that time he had one severe and two slighter attacks.

It has also been stated that attacks could be postponed after the appearance of the first signs of weakness by taking exercise, but that the subsequent attack which follows as soon as the patient goes back to bed is more severe in degree. It has not been possible to test this in regard to T. L., as the rule is for him to wake up at night so far paralysed that exercise is practically out of the question. He, however, gives a history of having, on waking in the morning and finding himself weak, succeeded in "walking it off"; but it is clearly open to question whether he is not in reality just recovering from, rather than just beginning, an attack, and he is very certain that this "walking it off" has not in any case been followed by a more severe attack.

*Relation of Attacks to Gastro-intestinal Functions.*

Some of the recorded cases have shown a relation between the action of the bowels and the onset of an attack, but no such relation has been observed in this patient. His bowels are usually opened once or twice a day, and this has been so during the whole of his stay in hospital; he has never suffered either from diarrhœa or constipation.

An attempt was made to determine whether alterations in the diet produced any effect on the frequency and severity of the attacks; and for this purpose he was kept for a time on a carbohydrate-free diet, and subsequently given large doses of glucose, together with the ordinary full diet, but neither alteration seems to have had any effect. On the other hand, there are certain indications of some disturbance of gastro-intestinal function in his history of vomiting and nausea in the early stages of an attack at the beginning of

his illness, and whilst in hospital he has on several occasions complained of nausea, but has not vomited. The tongue, also, in the attack is generally a little furred. The examination of the stools and urine has been carried out by Dr. Goodbody, and his report and conclusions are appended below.

*Relation of Attacks to Urinary Excretion.*

Acting upon the hypothesis, which is more fully discussed below under the heading of the pathology of the condition, that the exciting cause of an attack may be the failure to completely remove the toxic products of metabolism from the body, an attempt was made to ensure more thorough elimination by the production of diuresis. The method employed was the administration of large doses of soda-water and Imperial drink in addition to the ordinary amount of fluid taken with meals, and at the same time small doses of digitalis and potassium acetate. Previous to this treatment he had been having attacks at the rate of at least one per week; in the following three weeks he had no attack at all. In order to control this result, the amount of fluid ingested was then diminished to two pints all told, and the digitalis and potassium acetate omitted; but he had only two abortive attacks during the next fortnight, although the amount of urine voided averaged about twenty ounces less than before. He was then kept absolutely at rest in bed with the same diminution in the fluid part of his diet; on the following day he had an abortive attack, on the next a more severe one, and on the third day a still more severe attack with dilatation of the heart. The amount of fluid taken was then increased as before, and the mixture of digitalis and potassium acetate again administered, with the patient still at complete rest in bed; in the following six days he had no attack at all, even of an abortive character.

These observations are very striking, especially when it is remembered that on the two previous occasions on which he was kept in bed for six days he had four and three attacks respectively, and should they be confirmed by other

observers, ought very materially to help us to a true conception of the nature of this extraordinary disease.

### *The Blood.*

The blood has been examined, both in the free intervals and also during the height of an attack, but the number of red and white cells, amount of hæmoglobin, and the proportion of the different varieties of white cells has been found to be in each case well within the limits of the normal. No abnormal varieties of red cells, and no foreign elements have been seen in any of the blood films microscopically.

### *Muscle.*

A portion of the L. Sartorius was excised, when that muscle had almost completely lost its power of voluntary contraction in an attack, from which sections and photographs were kindly prepared for me by Dr. J. S. Collier, pathologist to the hospital. The great majority of the sections showed the condition represented in fig. 1, in which is seen the most extraordinary amount of fissuring in the individual muscle fibres, such as is certainly not seen in sections of normal muscle, prepared in the same way, viz., by hardening in Müller's fluid and embedding in paraffin. Sections hardened in formalin showed precisely similar changes. Fig. 2, however, represents photographs of sections of the muscle hardened in Müller's fluid, and embedded in celloidin. In these, although not entirely absent, the fissuring is comparatively very slight, and this fact tends to show that the fissuring is probably artefact in nature. In spite of this, one cannot but believe that there must be some essential abnormality in the muscle fibres to produce such uniform and unusual appearances.

### *Pathological Examination of the Urine and Fæces* (by Dr. Goodbody).

During one of the attacks, it was decided to investigate the condition of the urine in order to see how far it agreed with what was described by Crafts. For this purpose, the

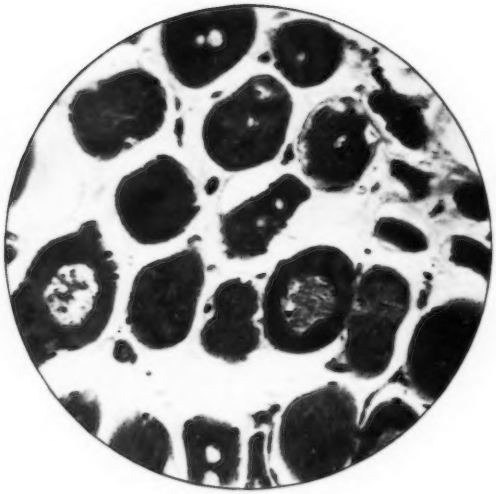

FIG. 1.

Transverse section of left Sartorius muscle excised during an attack, hardened in Müller's fluid and embedded in paraffin. In the centre of many of the fibres is seen a more or less circular fissure some of which contain some hyaline material.

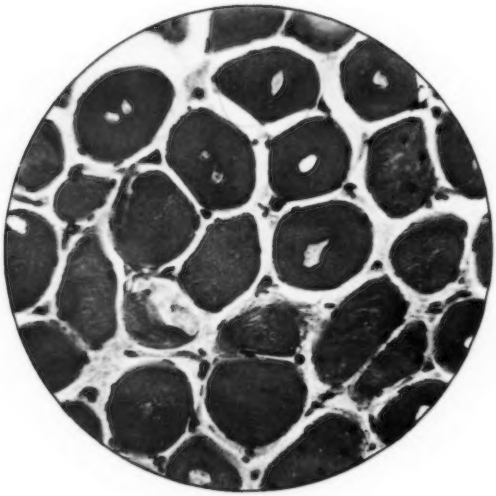

FIG. 2.

Transverse section of a portion of the same muscle hardened in Müller's fluid and embedded in celloidin. It will be seen that the fissuring although still present is much less marked.

total urine passed during the twenty-four hours in which the attack occurred was collected, and also that excreted during the succeeding twenty-four hours. For the purpose of comparison, a two-day period was taken about a fortnight later, in the interval between two attacks, and the urine of each day submitted to analysis in order to obtain a result as nearly approaching the normal as was practicable.

| | | Period of Attack. | | | Interval. | | |
|---|---|---|---|---|---|---|---|
| Urine. | Quantity | 430 | 1230 | 830 | 660 | 1660 | 1160 |
| | Specific gravity | 1020 | 1026 | 1023 | 1023 | 1019 | 1021 |
| | Nitrogen | 6·62 | 18·01 | 12·32 | 7·42 | 18·43 | 12·93 |
| | Urea | 11·91 | 31·88 | 21·90 | 14·52 | 32·44 | 23·48 |
| | Uric Acid | 0·31 | 0·90 | 0·61 | 0·32 | 0·85 | 0·58 |
| | Chlorides | — | — | — | — | — | — |
| | Phosphates | — | — | — | — | — | — |
| | Sulphates. Total | 0·77 | 4·73 | 2·75 | 1·60 | 3·92 | 2·76 |
| | Sulphates. Alkaline (A) | 0·69 | 4·40 | 2·55 | 1·48 | 3·69 | 2·59 |
| | Sulphates. Aromatic (B) | 0·08 | 0·33 | 0·20 | 0·12 | 0·23 | 0·17 |
| | Sulphates. Ratio A : B | 8·6:1 | 13·3:1 | 12·7:1 | 12·3:1 | 16·0:1 | 15·2:1 |

In dealing with the first period, that of the attack, it must be pointed out that on the first day the patient practically took no food, as the seizure lasted almost twenty-four hours. On the second day, he took a considerable quantity of milk. The quantity of urine excreted during the first day was small, amounting only to 430 cc. with a specific gravity of 1020. On the following day, the excretion rose considerably, as 1230 cc. was passed, while the specific gravity, notwithstanding the increase in the quantity of water eliminated, rose to 1026.

On the first day, the quantity of total nitrogen excreted in the urine was very low, only 6·62 grammes, while on the second day, 18·01 grammes were eliminated. Although, as already mentioned, some milk was taken on this day, still the quantity excreted was very large in comparison with the preceding twenty-four hours, and there appears to have been an increase in the metabolic processes, especially as 82·61 per cent. of this amount was excreted in the form of urea. On the first day also the proportion of the total nitrogen excreted in the form of urea was about the normal, being 83·96 per cent. The quantity of urea excreted on each day was 11·91 grammes and 31·88 grammes respectively.

The amount of uric acid excreted on the first day was 0·31 grammes, being about the normal quantity for a boy of his age. On the second day, there was a considerable increase in the quantity found (0·90 grammes), although it will be noticed that the amount of total nitrogen excreted in this form remained about the same.

On turning to the consideration of the sulphates in the urine, the small amount of proteid metabolism occurring in the organism on the first day is shown by the fact that only 0·77 grammes of total sulphates were eliminated. Of this amount, 0·69 grammes were excreted as alkaline sulphates, and only 0·08 grammes in the aromatic group. The ratio of the former to the latter was 8·6 : 1. On the second day, the great activity of the proteid metabolism is shown by the large quantity (4·73 grammes) of total sulphates excreted in the urine. 4·40 grammes of this amount was eliminated in the form of alkaline sulphates, while the quantity eliminated as aromatic sulphates was rather above the normal, and was 0·33 grammes. The ratio of the alkaline to the aromatic sulphates was 13·3 : 1.

On the two days of the second period, there was a great similarity in the excretion of the urine, 660 cc. being passed on the first day, and 1,660 cc. on the second day. The specific gravity, however, reverted to the normal course, diminishing from 1,025 on the first day to 1,019 on the second day.

The excretion of total nitrogen was also low on the first day, and only amounted to 7·42 grammes, and the proportion eliminated in the form of urea was high, being 91·32 per cent. On the following day the same marked increase in the quantity of total nitrogen excreted was observed, as 18·43 grammes were eliminated, the amount passed in the form of urea being 82·13 per cent. It should be mentioned that the patient took his food well throughout this period. The quantities of urea excreted were 14·52 grammes and 32·44 grammes respectively. The same diurnal differences were also observed in the elimination of uric acid, 0·32 grammes being eliminated on the first, and 0·85 grammes on the second day.

The lessened activity of proteid metabolism is well shown by the small quantity of total sulphates found on the first day in the urine (1·60 grammes). 1·48 grammes of this amount was eliminated in the form of alkaline sulphates, and only 0·12 grammes in the aromatic group. The ratio of the former to the latter was 12·3 : 1. The quantity of total sulphates excreted on the second day was 3·92 grammes, so that the metabolic activity of the organism was much increased. Of this quantity 3·69 grammes were eliminated as alkaline sulphates, and 0·23 grammes in the aromatic group. The ratio of the alkaline to the aromatic sulphates was 16 : 1.

From the above, it is seen that there was a great similarity between the two periods, although the quantities found were slightly larger in the second period.

If the averages of the two periods be compared, it will be seen that no indications as to either diagnosis of the attacks or to treatment can be drawn, since the various substances analysed for give practically the same results. The principal difference is that the average excretion of urine per diem was 830 cc. in the first period as compared with 1,160 cc. in the second period. This appears to give a clue to the appropriate treatment, namely, diuresis, especially if—as might be concluded from the analysis of the first day of the second period—the patient was on the verge of an attack. The average specific gravities were rather above the normal, being 1,023 and 1,021 respectively.

The average excretion of total nitrogen was practically the same, 12·32 grammes and 12·93 grammes, while the proportion eliminated in the form of urea was 83·29 per cent. in the first period, and 86·73 per cent. in the second period. Despite the daily variations observed in the excretion of uric acid, the averages of the two periods (0·61 grammes and 0·58 grammes) agree closely.

On turning to the consideration of the total sulphates in the urine, it will be seen that the average of the first period was 2·75 grammes, and of the second period, 2·76 grammes. Of the above quantities, 2·55 grammes were eliminated as alkaline sulphates in the first period, and 2·59 grammes in the second period, so that these averages also closely agree.

The aromatic sulphates averaged 0·20 grammes and 0·17 grammes respectively, and the average ratio of the alkaline to the aromatic sulphates was 12·7 : 1 in the first period and 15·2 : 1 in the second period.

Neither albumen nor sugar was found in the urine on any of the four days analysed.

Opportunity was also taken on each day to test the toxicity of the urine according to Bouchard's method. The urine of the day on which the attack occurred was injected into the external jugular vein of a rabbit weighing 1·750 kilos., which had been previously anæsthetised, and death occurred after 58 cc. had been injected, so that 31·1 cc. were used per kilo. body weight. In this case, the secondary dilatation of the pupil usually observed was very slight, and there was also no diuresis. Previous to death, only extremely slight convulsions were observed, and coma lasted to the end, as the heart apparently was paralysed before the convulsions reached their ordinary severity. The small number of cc. used per kilo. indicates that some toxin of a paralytic nature was present in excess.

110 cc. of the urine of the following day was injected into the same vein of an anæsthetised rabbit, weighing 2·250 kilos., the number of cc. per kilo. body weight being 49. In this case the customary sequence of events was observed, namely, contraction, followed by extreme dilatation, of the pupil, diuresis, and, immediately before death, several well-marked convulsions. There is, therefore, evidence of increased toxicity of the urine of this day also, though not so marked as on the previous day.

On the first day of the second period, a rabbit weighing 1·850 kilos. was used, and canula was inserted into the external jugular vein, after the animal had been anæsthetised. On this occasion, 121 cc. were used, and therefore, 65 cc. per kilo. body weight was necessary to cause death. That is to say, about the normal quantity, according to Bouchard's statement. The customary phenomena were also observed in this case.

Owing to an accident, we were unfortunately unable to make a similar test with the urine of the second day of this period.

From the above results, it will be seen that in this patient there was a great increase in the toxicity of the urine during the attacks, and that the toxin or toxins were of a paralytic nature; but no attempt was made to isolate it or them.

Following the procedure given by Crafts (18), extracts of the fæces passed immediately after an attack and in the interval were made by Brieger's and Otto's methods and the results obtained were as follows:—

One gramme of each extract of the fæces passed immediately after an attack was injected into the subcutaneous tissue of a guinea-pig and the animal was carefully observed for the ensuing forty-eight hours. No paralytic symptoms whatever were observed, and all the animals appeared perfectly well with the exception of one which died from sepsis one week later.

Of the animals, injected similarly with extracts of fæces passed during a healthy interval, one died almost immediately, but none of the others showed any symptoms at all.

## CRITICAL DIGEST.

### *Historical.*

The first undoubted case of this disease was published by Hartwig (1) in 1874, under the title of "Intermittent Spinal Paralysis," in his inaugural address at Halle. He gives no details as to family history, but notes that during the attacks the electrical excitability of the muscles is almost entirely suppressed. A probable case was published without much detail by Samuelsohn (2) in 1876. In 1882 the first evidence of the familial nature of the disease was noted by Schachnowitsch (3), who published a case whose father had been similarly affected. In 1885 appeared a most excellent monograph by Westphal (4), giving a detailed account of the clinical phenomena to which but little has been added since. In this paper we also find the first mention of temporary dilatation of the heart. The following year Cousot (5) published the first instance of marked family affection,

and gave a digest of previous papers. This was rewritten and amplified in 1887 (6).

The next paper of importance was that of Goldflam (8) in 1890, which is preliminary to a more detailed account of the same material which appeared in 1891 (10). This is very full and deals largely with the electrical phenomena, and also includes a very excellent analysis of all previously recorded cases. Oppenheim (11) in 1891 gives another full account, particularly of the electrical reactions of the case published by Westphal in 1885. Goldflam (13, 14) contributes two further papers in 1895 and 1897, giving some fresh cases, and also the results of investigations carried out with a view to determining the ætiology of the condition.

In 1898, Taylor (15) published two cases belonging to a family in which the disease dates back for five generations, and gives an excellent *resumé* of the whole of the previous literature, and it is to this paper that I am indebted for all the earlier references. Since that time three papers by American authors have appeared, each publishing new cases. Mitchell (16), 1899, carried out some important examinations of the blood, urine and fæces, but with negative results. Putnam (17), 1900, gives most of his article to the discussion of the question of inhibition; and lastly, Crafts (18), 1900, asserts that he has found a toxin in the fæces, which on injection into animals produced temporary paralysis, but he does not appear to have controlled his experiments.

Besides the above papers, cases have been recorded by Greidenberg (7), Pulawski (9), and Hirsch (12).

### *Clinical Phenomena.*

The clinical manifestations of this disease are so constant and similar in all cases that it is unnecessary to describe them again as a whole; the case described above will serve well as a type. But the main features may be briefly summed up as follows: Periodic attacks of flaccid paralysis in an otherwise healthy individual, of varying duration from five or six to seventy-two hours, during which there is a

gradual and progressive onset, leading in complete attacks to absolute paralysis of all four extremities, neck and trunk, but not affecting, as a rule, the muscles supplied by the cranial nerves. Proceeding *pari passu* with this loss of power there is loss of muscular excitability to electricity and percussion, and abolition of all reflexes in the affected parts. After a variable period this condition gradually disappears, and the affected person once more becomes apparently sound and healthy. There is never at any time any loss of consciousness or impairment of mental functions, nor any demonstrable change in any afferent path.

Some of the important points may now be discussed in more detail.

*Age of onset of first attack.*—This has varied between 6 and 24 years; in one case, recorded by Goldflam, the mother of two children similarly affected, had only one attack, and this occurred at the age of 36 years, but if we exclude this the average age at which the disease has appeared, in the cases where this point is definitely stated, is 14 years.

*Sex.*—The two sexes are about equally affected.

*Time of onset.*—This has been almost invariably at night, the patient waking after a variable period of sleep to find himself more or less paralysed. Attacks, however, do sometimes start in the daytime, especially, as I have found, if the patient is kept continuously in bed. Mitchell obtained the history that one of the ancestors of his patients had sometimes to get off his horse when riding, and "have a paralysis." Besides these attacks, what appear to be abortive attacks have been noted by several observers as occurring during the daytime, consisting merely of slight weakness of the legs and possibly arms, lasting half to one hour and then passing off altogether. Possibly some of the attacks reported as having been walked off were of this nature.

*Periodicity.*—The intervals between the attacks as a rule are irregular; at first amounting to months, they may steadily diminish until the attacks occur every week or even oftener, and this condition obtains well on into middle life, when the intervals tend again to increase.

*Premonitory symptoms* have been in the majority of cases entirely absent, but Westphal and Cousot describe pricking in the legs, formication, muscle pain and thirst as occurring before the onset of an attack. In one of Goldflam's cases there was itching on those evenings when no attack occurred, coming on about the usual time for the onset of the attack, but on the evenings when he had an attack no such itching was felt. Hirsch describes a heavy tired feeling in the legs as occurring for some days before the onset of an attack. In the later recorded cases no such prodromata have been observed.

*Order in which the muscles are involved.*—This appears to be practically the same in all cases, the weakness beginning in the legs, extending then to the arms, and lastly to the trunk and neck. The more distal muscles, such as those of the fingers and toes are always the last to become completely paralysed. Cousot records one case in which the attacks began in the arms on a few occasions, and in one of Goldflam's cases, too, the order was hands, arms, legs. The arms were most, though not first, affected in one attack in my own patient. The order of recovery appears to be the reverse of the order of onset.

*Cranial nerves* have been unaffected in nearly all cases, but in some of the very severe attacks changes have been observed. One of Taylor's patients gives a history of a somewhat doubtful attack which was preceded by loss of consciousness, and said to be due to taking "some headache medicine." In this attack, which was very severe and lasted three days, the face was involved. Crafts records difficulty in opening the mouth, Hartwig and Cousot difficulty in speaking and swallowing. Hartwig also observed inequality of the pupils and even myosis. In my own case partial bilateral ptosis and dilation of the right pupil have occurred twice while under observation.

*Respiration* is always affected in complete attacks, in that the intercostals and extraordinary muscles of inspiration are paralysed. The diaphragm, however, seems to escape, but it seems probable that it is weaker than normal, because, as noticed by most observers, respiration is very

shallow, and there is complete inability to deepen the breathing. Goldflam records that on one occasion there was dangerous asphyxia, and in the doubtful attack alluded to above in Taylor's patient, artificial respiration had to be performed during one night.

*Heart.*—The affection of this organ has been now recorded by so many observers that there can be no doubt as to its occurrence. This point is one of very great importance as giving some indication of the seat of the change which results in the paralysis. The first allusion to any change in the condition of the heart was made by Westphal, who described slight temporary enlargement. Oppenheim had the opportunity of examining this patient again six years later, and described the heart in some severe attacks as being irregular in action, with a systolic murmur at the apex and slight accentuation of the second sound at the base, while the first sound was feeble and the pulse slow; there was, however, no enlargement of the area of cardiac dulness. Since then Goldflam and Mitchell have found systolic murmurs without enlargement of the area of cardiac dulness. Hirsch and myself have found enlargement of the area of dulness, with some impurity of the first sound at the apex, but no definite murmur. Crafts describes the pulse as being sometimes dicrotic, but with no murmur or cardiac enlargement. From these observations it will be seen that the change consists in dilatation with or without definite regurgitation through the mitral valve.

*Electrical changes.*—The loss of excitability of muscles to both faradism and galvanism which takes place during an attack has been confirmed by all observers, and is one of the most characteristic features of the disease. Mitchell added to our knowledge of the electrical condition by using needles thrust directly into the muscles as electrodes, and found that even then a very powerful current is needed to produce any contraction. This point will need further discussion later under the pathology of the disease. All observers agree that the change is purely a qualitative one and that it is proportional to the loss of voluntary power.

In the intervals between the attacks the majority of

patients have reacted quite normally to both currents directly and indirectly. Goldflam, however, has found permanent changes. In two brothers affected with family periodic paralysis he found partial R.D. in the small muscles of the hand, *i.e.*, diminished faradic excitability, increased galvanic excitability with A.C.C., equal to, or even greater than K.C.C. He lays great stress upon this as showing some definite changes to be constantly present in the muscles; but the fact that these particular muscles were not specially affected during the attacks, either with respect to early onset or degree of paralysis attained, hardly bears out this supposition. The vast majority of evidence points to the electrical change, which takes place in the attacks, being as temporary as the loss of motor power; both being probably due to the same temporary cause.

## *Ætiology.*

*Heredity.*—The familial nature of the disease is forced upon one's notice by the cases recorded by Cousot, Goldflam, Taylor and Mitchell, who give the numbers of relatives affected as five, nineteen, eleven and seven respectively—a total of forty-two cases in four families. Goldflam and Taylor have both traced the disease back through five generations. Of the remaining cases three members in one family have been recorded by Goldflam and two by Schachnowitsch and Hirsch, while all others appear to be sporadic. Transmission of the disease takes place through both males and females, and sometimes spares one generation to reappear in the next.

Heredity thus plays a most important part in the causation of the disease, but it has not been shown that the affected families are subject to any other form of hereditary neurosis or myopathy.

*Specific fevers* have been suggested as exciting causes of the disease, especially among the earlier writers. Malaria more particularly was quoted, probably because of the periodicity. The majority of patients, however, have never suffered from malaria. Scarlet fever and typhoid have been

noted in the previous history of some cases, but although they might possibly act as the exciting cause of symptoms of this disease, there is no evidence to show that they have any effect in producing the disease itself.

*Exciting causes of attacks.*—In all cases attacks may come on without any assignable cause, but three conditions have been quoted which have appeared to precipitate attacks.

The first and most important of these is physical over-exertion, and it has been so strongly supported by nearly all observers, that there can be little doubt as to its accuracy. In Mitchell's case, and in the one described above, no such connection could be demonstrated.

This question will be further discussed under the pathology.

Indiscretions in diet and gastro-intestinal trouble have also been accredited with the power of exciting attacks. Hirsch's patient attributed his to the drinking of tea or spirits overnight, while Crafts states that his patient had learnt to eschew jams and cheese. Careful observations on the diet have, however, failed to confirm this view. Constipation and diarrhœa are recorded as preceding the onset of an attack, and Crafts goes as far as to say that one or the other, generally the former, is an almost invariable precursor in his patient. Other observers, however, have failed to observe this association.

The third factor, emotion, has only been recorded by Cousot, and is hardly noticed by other observers. It would, however, appear to have occasionally excited attacks in the case which forms the text of this paper.

## *Pathological Anatomy.*

In the intervals between the attacks, all persons suffering from this disease have been practically healthy, and up to the present but little has been discovered abnormal during the periods of paralysis.

The *blood* has been examined by Goldflam, Taylor, Crafts and Mitchell, with almost entirely negative results.

The first three observers all record a slight relative lymphocytosis during the intervals, but the change is almost within the normal limits, and it is questionable if any significance can be attached to it. Examination of the blood cells in Mitchell's and my own case revealed nothing abnormal. A leucocytosis during an attack was found by Klein who examined one of Goldflam's patients, but this has not been confirmed by others. The toxicity of the blood serum was carefully estimated by Dr. Stengel in Mitchell's case, but found to be within normal limits.

*Muscle.*—Specimens have been examined by Goldflam and Crafts. The former describes a condition of increased diameter of individual fibres, together with some vacuolation, and to this he is inclined to ascribe the permanent electrical change he has found. Crafts describes much the same condition, and adds that there is a distinct increase in the amount of fibrous tissue; this finding is, however, discounted by the fact that he was using the gastrocnemius muscle. The vacuolation of the fibres is distinctly interesting when compared with the almost identical results obtained from the case described above; this change, which I believe to be artefact, would appear to indicate some abnormality in the muscle, rendering it more liable to shrinkage and alteration in being prepared for microscopic examination. When one considers the short duration of the paralysis, it seems hardly possible that any very gross changes in the muscle should be found.

*Urine and fæces (by Dr. Goodbody).*—The first reference of any importance as regards the examination of the urine was made by Goldflam. He estimated the toxicity of the urine by Bouchard's method, and found that, during the attacks, there was a distinct increase in the urotoxic coefficient, the increase, in some cases, being nearly fourfold. His first idea was that the poisonous substance was in the alloxuran group, but he afterwards came to the conclusion that this was not the case, as the results of analysis practically show equal amounts of this substance, both during the attacks and in the intervals. The final conclusion that he arrived at was that the active principle was of the nature

of a toxic substance formed in the intestinal tract, but he made no attempt to isolate this substance, or substances, as described.

In Craft's report of the case investigated by him, there is no difference to be noticed in comparing the analysis of the urine voided during the attacks, and that passed during the interval. He found also an increased toxicity of the urine during the paralytic stage, but was unable to isolate the active toxic principle. Some experiments were carried out in connection with his case, in order to ascertain, if possible, whether any toxic principle could be isolated from the fæces. Extracts of the fæces were made in several different ways, and these extracts were injected into guinea-pigs, with the result that temporary paralysis, lasting about twenty-four hours, was observed in these animals which were inoculated with extracts of the fæces during the period of attack. In this case also, no success attended any attempt to isolate the toxic principle. So far, we have been unable to confirm his results on this subject.

### *Pathology.*

The earliest opinion expressed as to the nature of the condition was that of Hartwig, who assumed that the paralysis was due to hyperæmia of the spinal cord, with temporary increase of serous exudation. Samuelsohn suggested that the paralysis was hysterical, but this may at once be excluded in the presence of such definite and characteristic evidence as the loss of reflex and electrical excitability. Westphal in 1885 was the first to suggest that the disease was due to some form of toxæmia, a view that was strongly upheld by Goldflam in 1890, who added that it was probably an auto-intoxication. This theory has been accepted by all observers since, the only variance of opinion being as to the *point d'appui* of the toxin in producing the palsy. Goldflam's own theory would place the lesion in the muscle fibres and motor nerve endings, a conclusion to which one seems forced by the electrical changes. The condition of the muscles with regard to electrical excitability is that of muscle which has gone beyond the stage of mere separation

from its motor centre in the cord, such as is seen after recent section of the nerve fibre, or destruction of ant. cornual cells, and has arrived at a stage which corresponds with the functionally dead muscle seen in very old standing cases of infantile paralysis. This view is also strongly supported by the fact that the heart undoubtedly suffers, though to a less extent than the skeletal muscles, and even more so by the probability, as pointed out by Mitchell, that the muscle of the vessel walls suffers also. One point, however, which does appear difficult to explain, if we regard the paralysis as due to poisoning of the muscle fibres, and upon which very little stress has been laid, is the almost universal escape of the muscles supplied by the cranial nerves. There is no known anatomical difference that would account for their escape, and to suggest any selective action for a toxin, which otherwise acts so universally, is not in any way satisfying.

The only other notable theory, which was first enunciated by Cousot in 1887, and has recently been reformulated by Putman in 1900, suggests that the toxin, whatever it be, produces its effect by exciting the inhibitory action of cerebral or spinal centres. Such a suggestion it is impossible to disprove, seeing that we know little or nothing of the power that is called into action ; further it is unnecessary as most of the phenomena are explicable without it.

One other important point remains to be considered, viz., as to the nature and origin of the toxin, the existence of which is practically admitted by all. Here we are verging into the realms of pure hypothesis, but certain points are worthy of discussion. In the first place two views are possible as to its nature and origin. (1) It is an entirely foreign substance, *i.e.*, a specific poison ; (2) It is an increase in the amount of some of the toxins normally present in the body as a result of metabolism ; the accumlation being due either to increased production or diminished elimination, or both.

With regard to the presence of a specific toxin, all that can be said, if we neglect Crafts' unsupported findings, is that all attempts to demonstrate such poison, either in

the blood, urine or fæces, have signally failed. When, however, we come to consider the question of excess of what may be termed the normal toxins, we have some evidence of importance in that the urine shows an increased but otherwise unaltered toxicity.

The undoubted excitation of attacks by muscular fatigue recorded by so many observers here leads us to question whether the increased toxin is not that produced by muscular work. The result of severe exercise in an ordinary healthy person is a condition of loss of power in the fatigued muscles, which soon passes off. May it not be that family periodic paralysis is produced in this way in persons whose muscles are predisposed by heredity or otherwise to suffer more from the effects of such toxins. Having reached this point, we have still to explain the periodicity, and also the fact that attacks in the case described above were more frequent in bed than when taking exercise. The other factor in the accumulation of the poison in the blood is a diminution in the excretion and the suggestion may be made that for some reason, such as the complete rest is bed, excretion is not as complete as it should be. This suggestion would appear to be borne out by the results of diuretic treatment described above.

If these points are admitted it may next be asked why does the patient recover from the attack, seeing that the rest is still more complete and there is partial suppression of urine? The fact that urine voided immediately after an attack is increasedly toxic, and the copious sweating that is seen in many of the cases may serve to explain this difficulty, as we must assume that metabolism is at a very low ebb whilst the muscles are practically dead, and yet at the same time there is a slow excretion of toxin going on in the urine and sweat which would result in the course of time in a return to the normal condition.

A comparison with the disease described under the name of myasthenia gravis may render this hypothesis, viz., the accumulation of the products of metabolism of muscle more tenable, for there we find a condition in which muscle, as

the result of work, loses both voluntary power and faradic excitability, recovering again more or less completely after rest. It must be pointed out, however, that in myasthenia gravis, although the faradic excitability may entirely disappear for the time being, yet the muscles still react readily to galvanic stimulation. This difference serves to clearly differentiate the two diseases, the explanation being probably that in family periodic paralysis the muscle fibres are affected, while in myasthenia it is the motor nerve endings that suffer; the clinical history of the two conditions is also quite distinct. Yet in spite of these differences there is a resemblance which will probably lead to the two diseases being classed together under the same clinical and pathological group.

### *Classification.*

Until we know more of the pathology of the disease it is impossible to class it accurately with other diseases. The periodicity, together with the extraordinary change in the electrical reactions and reflexes, and the entire absence of all sensory symptoms, make the actual diagnosis easy. Goldflam, relying on the permanent electrical changes he has found, classes the disease with the myopathies. Taylor is more inclined to group it with the congenital myotonias. Both these views are probably correct in that there is almost certainly some hereditary, or at any rate congenital difference in the muscle fibres, causing them to suffer from the effects of the toxin; but the resemblance is closer, as pointed out above, to myasthenia gravis. The periodicity of the disease would also lead us with Mitchell to relate it to such conditions as migraine, in which it seems probable there is some form of periodic auto-intoxication, also markedly hereditary in character.

### *Prognosis.*

The general opinion seems to be that the number of attacks tends to diminish towards middle age and sometimes they cease altogether. Goldflam mentions one case in which the attacks ceased at the first confinement. Life does not appear to be shortened by the disease, nor does death appear

to have occurred as a result of the attacks, except possibly in the case of the father of Schachnowitsch's patient.

### *Treatment.*

Has hitherto proved useless. Numerous drugs have been tried, such as quinine, bromide, arsenic, strychnine, &c., but all have failed. Electrical treatment, massage, &c., have also proved quite unavailing.

From my own observations, however, which require confirmation, I would recommend a regular, non-exciting life, with plain, simple food and moderate physical exercise. Diuresis should be promoted by the exhibition of large quantities of water, or as a pleasant and efficient substitute, imperial drink, while the bowels should not be allowed to become constipated. Turkish baths occasionally may be of value, but I cannot speak from experience. Drugs probably are not of much value, but if the attacks are frequent some digitalis and potassium acetate or citrate may be found useful.

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* *The original papers were not obtained, but a good abstract is given by Goldflam.*

# THE NERVE-CELLS OF THE HUMAN POSTERIOR ROOT GANGLIA AND THEIR CHANGES IN GENERAL PARALYSIS OF THE INSANE.

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ALTHOUGH there is a considerable amount of literature upon the changes in the cells of the posterior root ganglia in general paralysis of the insane, there still exists much diversity of opinion as to the extent to which those cells are affected, some authors describing advanced and destructive changes in the cells, while others are of the opinion that the affection is very slight.

It is worthy of note that before describing the changes to be found in general paralysis no one has attempted to give an account of the normal intimate structure of the posterior root ganglion cells; and it seems to us that a minute description of those cells, studied by the most modern methods now at our disposal, is an absolute necessity, because, as we hope to show, there are several types of cells which vary very markedly in size and in the arrangement of the chromophile elements, so that without a knowledge of the normal features one cannot attempt to describe the modifications which the cells undergo in the course of a disease such as general paralysis of the insane.

Early in our work it became evident to us that the older methods of fixation and hardening were utterly useless for the study of such a delicate cell as that contained in the spinal ganglia, and so we found it necessary to finally discard such fixatives as formalin and graduated alcohol.

As a result of adopting a new and reliable method of fixation, we have proved to our satisfaction that work conducted by the methods formerly used is full of artificially produced appearances, which in many cases have been mistaken for evidences of a morbid process. What those changes are we shall show before describing the changes found in the posterior root ganglia of general paralytics. But in the first place let us see how our knowledge stands with regard to the normal structure of the posterior root ganglion cells.

Before entering on a description of the types of cells found in the normal human posterior root ganglia we must refer to the work which has of late been done on the ganglia of the lower animals.

For several years it has been recognised that there were cells of different sizes in the posterior root ganglia, but, until comparatively recently, no attempt was made to classify the cells beyond the use of the terms "large" and "small." During the last five years, however, several observers have given some attention to the subject, and have classified the cells according to their size and to the arrangement of the chromophile elements within the cell.

Lugaro has summarised the literature on the subject and has given concisely the views held by various observers in his paper published last year; we shall refer to this fully later.

Dogiel, Ramon y Cajal and Oloriz recognised, when using Ehrlich's "*intra-vitam*" method, that there were large clear cells and small obscure cells.

Nissl, in 1897, described four types of cells in the posterior root ganglia of the rabbit; he distinguished them as follows:—

(1) Cells with large chromophile elements arranged concentrically around the nucleus.

(2) Cells having a single layer of elements arranged at the periphery, a thin clear zone just below this free from chromophile elements, and another clear space in the neighbourhood of the nucleus.

(3) Cells with a thin peripheral layer and a broader peri-

nuclear layer of large elements, and between these two a band of smaller elements, with sometimes some larger elements mixed with them.

(4) Cells somewhat similar to the preceding, but more or less indeterminate in character.

Van Gehuchten and Nelis, in 1898, distinguished the small and obscure cells from the large clear cells, and by the relative amounts of chromophile elements they distinguished numerous types which, they considered, were united by intermediate forms. They described the two types most commonly met with as being rich in chromophile elements, but in one these were large, irregular in shape, and scattered through the whole of the protoplasm of the cell; while, in the other variety, they were in the form of fine granulations uniformly distributed throughout the cell excepting a narrow clear peripheral zone.

Their third type included cells with a few fine irregularly shaped elements.

Next they described cells with large fusiform elements arranged concentrically around the nucleus.

They then mentioned a rare type in which a few large irregularly shaped chromophile elements were arranged exclusively around the nucleus; and, lastly, a still more rare type, whose elements were divided into two bands, one at the periphery and the other around the nucleus, and between the two there was a zone free from chromophile elements.

Cassirer in his description of the cells of the posterior root ganglia of the rabbit mentioned four types:—

(1) Large clear cells with the nucleus generally central, but sometimes displaced to the periphery; the elements in these were arranged around the nucleus, and at the periphery in concentric layers, and there was a narrow clear zone at the periphery, and a narrower one around the nucleus.

(2) Medium-sized cells, for the most part clear, with a large nucleus generally central, but sometimes excentric; around the nucleus there was first a zone of large chromophile elements, then one of very fine chromophile elements, and again at the periphery a zone of large elements.

FIG. 1.

Two large clear cells, with central granuliform elements and a single peripheral ring of large chromophile elements. Note the perinuclear space. *Lugaro's type, No.* 2. Zeiss, apochrom., obj. 8 mm., oc. 4.

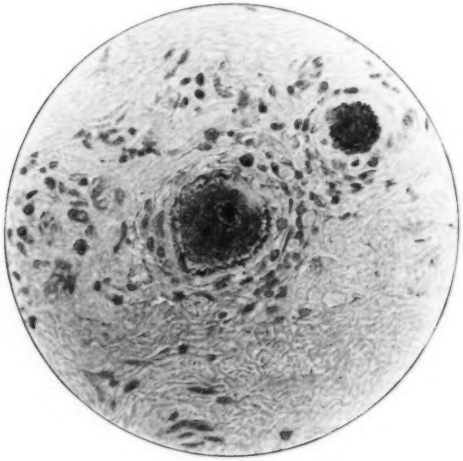

FIG. 2.

Early stages of chromatolysis in type 2. The nucleus is slightly excentric and the peripheral edge of the central granuliform mass is beginning to break up. Note the persistence of the peripheral chromophile ring. Zeiss, apochrom., obj. 8 mm., oc. 4.

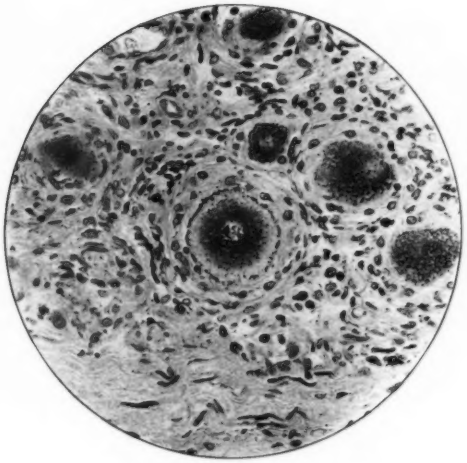

FIG. 3.

More advanced stage of chromatolysis in type 2. The central chromophile mass is very degenerated at its periphery and there is a clear space left between it and the large peripheric chromophile elements which are still well preserved. The nucleus here has retained its central position. Zeiss, apochrom., obj. 8 mm., oc. 4.

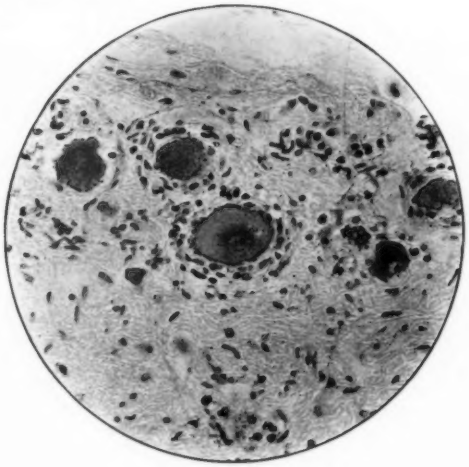

FIG. 4.

In this example of type 2 the central chromophile mass has disappeared with the exception of a few granules around the nucleus. Note that the peripheric chromophile ring still persists at this late stage of chromatolysis. There is a small dark-staining band of chromophile substance attached to the outer wall of the central side of the nucleus. Zeiss, apochrom., obj. 8 mm., oc. 4.

(3) Cells as large as the last, but of irregular shape, with a smaller nucleus, often excentric, and the elements indistinct because of the staining of the fundamental part of the cell.

(4) Small cells with a relatively large nucleus, with the elements arranged irregularly and with the fundamental part of the cell stained. Sometimes in these cells two nuclei were seen.

Cox also in 1898 published a paper in which he described the cells in the posterior root ganglia of the rabbit, but he differed from the above-mentioned authors in that he considered that the types of cells were clearly distinguished from each other, and he failed to find any intermediate forms between the various types.

He mentioned two types, and the first of these he divided into two sub-types, cells large and cells small.

In the large cells of type 1 the chromophile elements were not large, they were of irregular shape and only at the periphery did they assume an elongated form ; no concentric arrangement was seen excepting at the periphery and here there was only one layer so disposed. The nucleus was situated in the middle of the cell and was rarely double.

The small cells of type 1 were distinguished by the fact that the fundamental substance between the chromophile elements had a tendency to stain more or less deeply. The elements were distinct, but always much smaller than those in the larger cells.

The cells of type 2 had elongated chromophile elements arranged in layers, some layers were concentric around the nucleus, and others were concentric around the central point of the cell. The nucleus was always excentric, often markedly so.

He then referred to the different appearances which this type of cell presented in sections which were made in different planes, and showed that in one section the nucleus might be near the centre and in another placed at the extremity of the cell.

It will be seen that there are considerable differences

between the descriptions of these cells given by the above mentioned authors; these differences have been cleared away, and in fact the classification of the types of cells met with in the posterior root ganglia has been placed on a firm and scientific basis by Lugaro in his valuable paper published last year.

Working with a new and improved technique, which will be described fully later in this paper, he divided the cells in the posterior root ganglia of the dog into five types, quite distinct from each other and having no intermediate forms. His first type consisted of clear cells, the largest in the ganglion, with fine granuliform chromophile elements scattered diffusely throughout the cytoplasm, and only a little increased in size and density at the periphery, internal to a narrow limiting clear zone, which was entirely deprived of them; around the nucleus also there was a narrow clear zone which was free from any chromophile elements; the nucleus was large and clear and was situated in the centre of the cell (fig. 6).

In his second type he included clear cells of medium size generally, although some of them equalled those of the first type. In these cells the chromophile elements around the nucleus were a little larger and less crowded than in type 1; they were bounded externally by a zone of varying width in which there were few, if any, elements, and outside this there was a single layer of large elements. At the periphery and around the nucleus there was a well marked narrow clear zone. The nucleus was large and clear and was always central (fig. 1).

The third type Lugaro spoke of as "scure" or darkly-staining cells. Many of these were small, but others were quite of medium size; they were frequently irregular in shape. The chromophile elements were very minute in the central part, and slightly larger towards the periphery. The distinguishing feature of this type was that the fundamental substance of the cells was stained more or less deeply, and this was the more marked in those of larger size. It gave rise to the dark, undefinable appearance similar to that seen in partially differentiated cells.

Frequently there was considerable difficulty in defining the outline of the chromophile elements, owing to the deep staining of the fundamental substance. The nucleus also was deeply stained; it was central, and was not relatively so large as in the other types. The peripheral and perinuclear zones were present, but were less distinct than in the clear cells.

The fourth type consisted of small or medium sized cells, in which the chromophile elements were large, few in number, and regular in shape, and had numerous branches attached; they were arranged concentrically around the nucleus, and there was a well marked peripheral and perinuclear clear zone. The nucleus was large, clear, and was situated centrally in the cell (fig. 8).

His fifth type of cell, corresponding to the type 2 of Cox, included cells of medium and small size. Some of these were round, and others were decidedly oval in shape. The nucleus was constantly excentric, often markedly so. The chromophile elements were arranged in concentric layers around the central point of the cell; those at the periphery were large, cohering, elongated, and united to each other by fine branches; those in the central part were smaller and more irregular, but the concentric arrangement was maintained. The peripheral and perinuclear clear zones were quite distinct (fig. 10).

The above description is a picture of a section of one of these cells made in the direction of the long axis of the chromophile elements; when the section was made in a plane at right angles to this, the chromophile elements were seen to have an irregular shape, and they were connected by their branches so as to present a reticulated appearance; their size, the excentricity of the nucleus, and the concentric arrangement of the chromophile elements will assist one to recognise them.

Moreover, intermediate forms, in which the section was made obliquely to the long axis of the chromophile elements, were frequently seen. In some cells too, the nucleus was placed at one end of the cell, with layers of chromophile elements disposed concentrically around it, and at the other

pole of the cell there was a distinct spiral arrangement of the elements.

This cell clearly corresponds to the cell referred to by Lenhossek as being found in the frog, in which he spoke of this disposition of the nucleus and spiral as "centrosome" and "sphere," and he considered it a cell in process of reproduction.

Levi, however, in 1897, noticed a similar cell in the toad, and he showed that in this type of cell the nucleus, with concentric layers of chromophile elements around it, was normally situated at one pole of the cell, and that the other pole was occupied by a figure, which he described as a "spiral vortex of fibrils and chromophile elements."

The above are the five types of cells which Lugaro described in the posterior root ganglia of the dog.

In his article on the posterior root ganglia of the rabbit he included types 1 and 2 under one head, because he found that in the normal cells there were some points of similarity; and he also found that, in the course of their degeneration after section of the afferent nerve, they passed through the same definite series of changes, and only at the very commencement were they distinguishable.

At the beginning of our work on this subject, we examined the posterior root ganglia of lower animals with the view of confirming the findings of Lugaro, and we then directed our attention to the root ganglia in man.

We have cut sections of the posterior root ganglia of the cat, the dog, and the rabbit, and we can fully confirm the description of the types of cells given by Lugaro; and a careful examination of the root ganglia in man has shown that the same types of cells exist there also.

We have followed Lugaro's classification, because it is the most recent and the most complete, and because we consider that a comparison with all the descriptions given above might lead to some confusion.

Our normal specimens were obtained from cases of acute mania who died soon after admission into the asylum. We

feared that it would be impossible to eliminate the fallacies due to imperfect fixation and to *post-mortem* change, if we relied on tissues obtained from a general hospital.

## Cell Types in the Normal Human Posterior Root Ganglia.

In the human posterior root ganglia we have been able to separate and to distinguish five independent varieties of cells, which show differences both in the normal arrangement of the chromophile elements, and in the way in which they undergo modifications in their degenerative phases.

The most common type of cell met with is that which corresponds to Lugaro's first type. The cells in this type are large and clear; the chromophile elements are granuliform, and are scattered throughout the entire cell body; but at the periphery there is a slight increase in their size (fig. 6). Outside the chromophile elements there is a well marked clear peripheral zone devoid of chromophile substance, and around the nucleus which is central, there is also a similar well defined clear zone, called the "perinuclear space."

The next type in frequency is that which corresponds to Lugaro's second type in the dog. We find this cell is clearly distinguishable from the preceding by the large size of the peripheral chromophile elements, which are arranged in a single ring around the cell (fig. 1). Internal to this ring the chromophile material is granuliform, the individual elements being very minute and irregular in size.

The granules are usually slightly increased in number around the centrally placed nucleus.

The peripheral and perinuclear clear zones are again prominent features, as in the first type.

The third and last type of cell, in which the chromophile material is exhibited in the form of granules, is that termed by Lugaro the "scure" or darkly-staining cell. In the human subject we find a large and small variety of this type.

In the smaller cells the chromophile elements are very minute, with indistinct outline, and are scattered diffusely

throughout the cytoplasm. In the larger cells the chromophile elements are larger, and are arranged in two concentric condensations—one around the nucleus and the other towards the periphery. In both the fundamental amorphous substance stains deeply, and obscures to a large extent the chromophile material; the nucleus, which also stains deeply, is central. A perinuclear clear space is recognised with difficulty, but the peripheral clear zone can always be seen, though narrower than in the large clear cells.

The two remaining types, about to be described, are sharply defined from the preceding three varieties by the large size of the individual chromophile elements. The granuliform chromophile substance, which forms the main feature in types 1, 2, and 3, is replaced in types 4 and 5 by an element which is much larger and more distinct, but the shape and arrangement is not the same in the two types.

Under type 4 we find two varieties, one with small cells and the other with cells of medium size, and in these there are certain characteristics common to both. The chromophile elements are large and comparatively few in number; the fundamental achromatic substance is either unstained or only very slightly coloured; the nucleus is central, and the peripheral and perinuclear clear spaces, which we have mentioned as being common to all the types, are prominent features in these cells (fig. 8).

In the smaller variety the chromophile elements are smaller and a little more slender than in the medium-sized cells, and they are arranged concentrically around the nucleus.

In the medium-sized cells the chromophile elements are larger, and tend to assume a diamond or square shape, and they do not present such a complete concentric disposition as is seen in the smaller variety. Both varieties, therefore, of this type can be clearly differentiated from any of the preceding types by the large volume and the well-defined outline of the chromophile elements.

In the other type of cell, which corresponds to Lugaro's fifth type in the dog, the chromophile elements are as large as in type 4, but differ from them in their shape and in their

disposition around the nucleus. The nucleus is normally markedly excentric and frequently occupies a peripheral position, but it is always separated from the extreme edge of the cell by a narrow band of chromophile substance. The chromophile elements are long and slender in the large examples of this type (fig. 10), and they radiate from the nucleus in successive rings towards the opposite pole of the cell. The elements are more closely packed together around the nucleus, but further away the space between adjacent rings is greater. In the smaller vorticose cells the elements are a little thicker, relatively to their length, than those in the larger variety, but the same arrangement in the cell prevails.

Sections of these cells made in different planes exhibit the same pictures as those described by Lugaro in the cells of the dog.

Various authors who have written on the subject of the posterior root ganglia have drawn attention to the fact that the size of the cells varies considerably in the ganglia of the different regions of the cord, the great majority of cells in some ganglia being large and in other ganglia small; and they have suggested that as the cells differ in size in various ganglia, their function also must be distinct. We have found that the cells do vary in size in different ganglia, but in each ganglion every type of cell is present, and there can be no doubt that in the ganglia in which the cells generally are small, those cells which belong to the smaller types are reduced in size, as well as those which belong to the larger types, and we must assume that the same type of cell has the same function in every case. It is hardly correct, therefore, to say that the large cells are absent or relatively greatly reduced in number in certain ganglia.

Another source of fallacy lies in the fact that in certain ganglia almost all the cells along one side may be of large size. If a section was made along this side, practically only large cells would be seen; but if a section was made at right angles to this, the various types would be seen in their usual proportions. We have, therefore, found it necessary to cut sections right through the ganglion.

## The Perinuclear Space.

In the above description of the cell types, reference has been made to a perinuclear space, which forms one of the constant histological appearances met with in the nerve-cells of the posterior root ganglia.

This perinuclear space is worthy of special mention, in view of the importance now attached to the intracellular lymphatic system and its connections, as there seems to be a large amount of evidence to show that this space forms part of the canalicular system described by Donaggio, Holmgren, and others.

It is not our intention to enter into a description of the lymphatic canalicular system or of the endocellular vessels (Fritsch, Holmgren, and Adamkiewicz), as such is quite outside the scope of this paper; but we may be pardoned for dwelling on the perinuclear space a little more fully, as it might be questioned whether the appearance was really a normal feature of the cell, or an artefact due to the effects of hardening or shrinkage.

Below it will be seen that considerable trouble has been taken to select the best fixative for these delicate structures in order to eliminate as far as possible faulty fixation or shrinkage during the subsequent operations of hardening and embedding. But first let us look at the opinions to-day advanced as to the precise nature of this structure.

In connection with their work on the endocellular lymphatic canalicular system, Holmgren and Donaggio have observed and described a distinct perinuclear space, containing no chromophile material, into which the canaliculi appear to open, and Holmgren seems to consider that the perinuclear space is to be regarded as the centre of the endocellular circulatory paths. We have ourselves observed two or three of these canaliculi in some cells of the first type, but we have not yet seen any instances where they open into the perinuclear clear space. The canaliculi are seen as clear, sinuous bands, surrounded on both sides by chromophile elements. Confirmatory evidence of the existence of this structure is to be

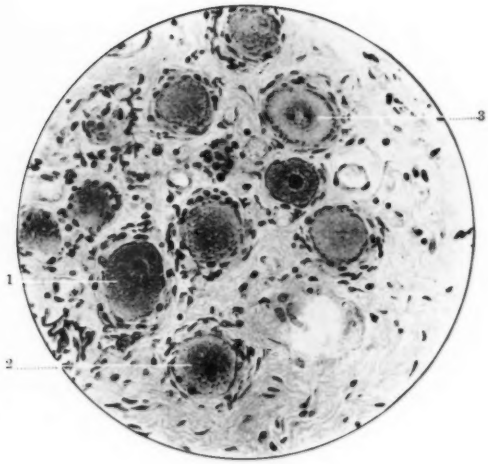


FIG. 5.

Note three cells of type 2 showing—(1) Early chromatolysis with excentricity of nucleus; (2) Degeneration of periphery of central granuliform mass; (3) Disappearance of central chromophile elements and persistence of peripheric chromophile zone. Zeiss, apochrom., obj. 8 mm., oc. 4.

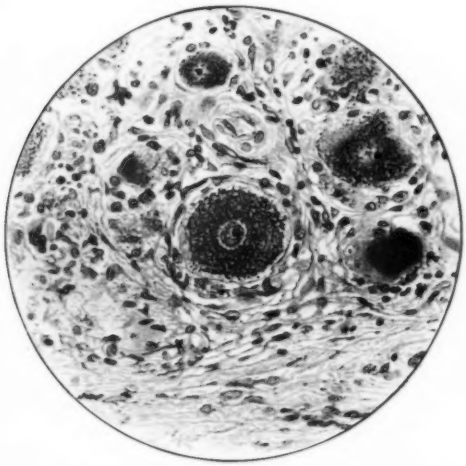

FIG. 6.

A large clear cell with granuliform chromophile elements. There is a slight increase in size of the elements towards the periphery but no definite prominent peripheric ring as in type 2. *This is Lugaro's 1st type.* Note the perinuclear and peripheral clear spaces. Zeiss, apochrom., obj. 8 mm., oc. 4.

FIG. 7.

Two large clear cells of type 1. In one there is a small localised deposit of pigment at one extremity of the cell; in the other there is a diffuse chromatolysis with marked excentricity of the nucleus. Zeiss, apochrom., obj. 8 mm., oc. 4.

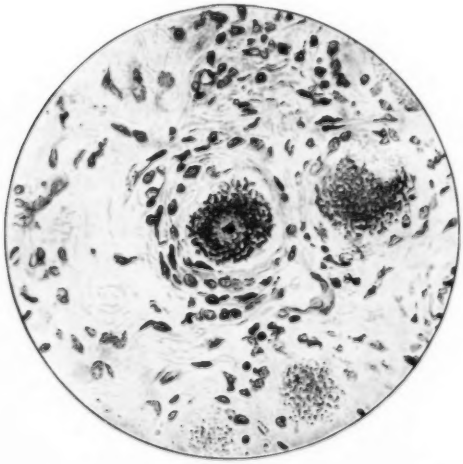

FIG. 8.

Medium-sized cell with large chromophile elements. Note the difference in size between the elements in this type and types 1 and 2. *This is Lugaro's 4th type.* Leitz, obj. 7, oc. 1.

found in the embryological researches of Fragnito, Colucci, Capobianco, and Piccinino, who, in working at the development of the nerve-cell, lay special emphasis upon the peculiar mode of development of the perinuclear space and the canaliculi.

Without going completely into a consideration of these authors' work, it is sufficient for our present purpose to note that they demonstrate the pluricellular origin of the nerve-cell, and in the course of their work they show how in the process of development the perinuclear space is formed, and that it is present at an early period of the existence of the cell.

The above-mentioned authors are agreed that the nerve-cell is formed from a primary neuroblast and several secondary neuroblasts, and that each neuroblast is surrounded by protoplasm.

The primary neuroblast becomes the permanent nucleus of the adult cell, while the latter become associated with it and undergo certain modifications to form the adult cell-body with its contents. Fragnito then shows that between the primary neuroblast and the secondary neuroblasts there is a space, which becomes the perinuclear space, and that this communicates with the spaces between the secondary neuroblasts, which become the canaliculi of the adult cell. In support of Fragnito's observations, Colucci affirms that the protoplasmic substance surrounding the primary neuroblast presents no true continuity with the nuclear wall. There is here a clear interposing ring in which there is a very faint, refractile, substance. As the surrounding protoplasm grows, the more evident does this clear ring become.

There can be little doubt, then, that the perinuclear ring is not an artificially produced appearance. It may be suggested that the reagents used in fixation and hardening caused retraction of the chromophile substance from the nuclear wall: but the observations of Colucci were made on fresh as well as hardened nervous tissues, stained with aniline dyes, and he found the same appearance in both instances.

### Peripheral Clear Ring.

There remains yet to be noted the peripheral clear ring, which also forms one of the histological features of all the cells types mentioned above. This ring varies in width according to the type of cell, being larger in the large cells and smaller in the small cells.

The chromophile elements do not reach the margin of the cell body, but terminate abruptly, leaving a clear zone around the entire cell. This is especially well seen in types 1 and 2. The outer margin of this zone is regular in outline and stains slightly more deeply, and so gives to the cell a well-defined edge and separates it sharply from the surrounding capsule.

In this peripheral clear zone no trace of chromophile substance can be seen, but minute fibrils are observed, with high magnification, to traverse it in all directions, giving one the impression of a fibrillar network. Between the external margin of the peripheral clear protoplasmic ring and the capsule enclosing the nerve-cell, there is a narrow pericellular space, crossing which one observes numerous minute, faintly-staining threads, which apparently run from the surrounding tissues into the peripheral clear zone of the cell body.

As to what these thread-like structures are, we hesitate to give a decided opinion; but the observations of Holmgren, Studnicka, Donaggio, and others, lead us to suggest that they may be of the nature of vascular or lymphatic structures.

Seeing that we have not employed any special technique or staining to warrant us in giving any definite view on this subject, we at present merely make a statement of their existence, while describing the peripheral clear ring which surrounds the ganglion cell.

### Fixation, Hardening and Embedding.

The choice of a suitable fixative and the subsequent hardening in alcohol are of the utmost importance in dealing

with such delicate structures as the ganglion cells under consideration.

It is interesting to note first the researches of Lugaro in this connection, and his results.

The following solutions were employed by him :—

(1) Equal parts of a saturated solution of corrosive sublimate and picric acid.

(2) Mann's solution (sublimate solution, picric acid and formaldehyde).

(3) Carnoy's fluid.

(4) Gilson's fluid.

(5) Nitric acid (5 per cent.).

(6) Cox's first mixture (saturated sublimate solution, 30 parts; osmic acid, 1 per cent., 10 parts; acetic acid, 5 parts).

(7) Cox's third mixture (saturated sublimate solution, 30 parts; formol, 10 parts; acetic acid, 5 parts).

The results were as follows :—In Cox's fluids some shrinkage occurred, while Carnoy's fluid fixes the centre better than the periphery of the cell. The mixture of saturated sublimate solution and picric acid, Mann's fluid and nitric acid gave the best results, not a single cell showing the least appearance of shrinkage.

In staining, Lugaro found toluidin blue the best stain, and in the process of differentiation he recommended absolute alcohol in preference to any essential oil. An accessory stain, such as erythrosin, he found to be harmful in its action, because it took place at the expense of the chromophile elements, the smallest of which tended to disappear. The selective properties of the stain differed with the fixing agent; with picric acid and sublimate and with Mann's fluid the smallest chromophile elements were projected with incomparable clearness on a transparent background, with nitric acid the colour was paler and the contour of the chromophile elements less distinct. Carnoy's and Gilson's fluids gave good results, but they were inferior to the others named. Delafield's hæmatoxylin gave good results after fixation in picric acid and saturated sublimate solution, and in Mann's fluid. We find that it is necessary to use this

stain in dilute solution (1-80), and good results are obtained after one hour's immersion.

In our own work we have used as fixatives,

(1) Mann's fluid.

(2) Saturated sublimate solution (Heidenhain).

(3) Saturated sublimate solution and picric acid.

(4) Nitric acid, 5 per cent.

We have found that the mixture of saturated sublimate solution and picric acid in equal parts gives us the best results with toluidin blue staining, although it may be mentioned that saturated sublimate solution alone is also a very good fixative.

It is impossible to attach too much importance to the special fixation and embedding methods which must be employed for the cells of the posterior root ganglion, because without such special fixation and staining, a recognition of the varieties or types of cells which comprise the ganglion is quite impossible.

The mode of preparation of the human posterior root ganglion, which we have finally adopted, after a somewhat lengthy trial, is as follows:—The ganglia to be studied must be obtained from the cadaver before *post-mortem* changes have had time to affect the cells even in the slightest degree. It can easily be understood that no matter how good the fixative employed may be, if *post-mortem* changes have set in an accurate picture of the nerve-cells cannot be obtained, and it can readily be demonstrated that the earlier the tissue is fixed the more do the results approximate to the appearances observed in animals whose ganglia have been fixed immediately after death.

The ganglion, which is carefully separated from the cord, is split into two pieces with a sharp razor, as we find that, without such an incision, penetration by the fixative is greatly delayed on account of the density of the capsule surrounding the ganglion and nerves. The division of these structures materially facilitates the rapid fixation which is so necessary, and allows the sublimate and picric acid to penetrate the ganglion from both periphery and centre.

The tissue is allowed to lie in the solution for three days —a less time scarcely suffices for the fixation of the larger ganglia; at the end of this time the fixative is poured off, and the process of hardening in graduated alcohol, commencing with 40 per cent., begins. When the hardening is completed the tissue is at once embedded in celloidin in the usual way, because we consider it preferable to keep the tissues in celloidin rather than to allow them to undergo prolonged immersion in alcohol. When required for sectioning, the embedding is completed by immersion in origanum oil and paraffin (equal parts) for twelve hours at a temperature of 45° to 50° C.; finally in paraffin alone for twelve hours, care being taken to reduce the deleterious effects of over-heating in the bath to a minimum.

The combined method of celloidin and paraffin embedding has been employed because it serves the double purpose of retaining the cells in position and at the same time allows of the thinnest possible sections.

It is necessary, in our opinion, to use celloidin as otherwise the cells may fall out of the section, leaving empty spaces, an appearance which will be referred to later.

We have laid special stress on the above technique because it seems to us that faulty fixation is entirely responsible for the spaces and shrunken cells, often described as signs of morbidity. Such so-called morbid appearances are very easily obtained in the posterior root ganglia of healthy lower animals, if one allows *post-mortem* change to become established, or if an inadequate fixative, such as alcohol, is alone used.

Tissues from the healthy animal have been treated by the various solutions mentioned above, as well as morbid tissues from the insane, and whereas the healthy cells, where faulty fixatives were used, exhibited a considerable degree of shrinkage, the cells in the morbid ganglia, treated by the most recent methods of technique, showed no sign of such an appearance.

When shrinkage of the nervous tissues does occur, whether from imperfect fixation, *post-mortem* change, or both combined, the appearances obtained are constant and

typical, and, as will be shown later, do not resemble in the slighest degree the pictures of true chromatolysis.

The first portion of the cell to be affected by the shrinking process is the peripheral clear zone previously mentioned. The pale achromatic substance forming this structure first loses its definite outline and deep indentations appear on its edge; as the change progresses, these indentations increase, until they reach the external limits of the chromophile part of the cell. On this stage being reached the cell is found to be without a proper peripheral clear ring, and this structure persists only in thick and thin deep staining bands uniting cell with capsule, and bridging across the artifically enlarged pericellular space.

In our description of the normal clear peripheral zone, it will be remembered that we described fine pale threads passing across the pericellular lymph space, and forming the only evidence of anatomical continuity between the nerve-cell and its capsule. It seems to us that it is along those threads that the cytoplasm shrinks, collecting on them, and thus giving rise to the thickened bands attached to the tissue surrounding the cell; it is only in this manner that we can see our way to account for the disappearance of the pale clear peripheral zone, which we know exists in the normal unshrunken cell, and for the development of the bands which occupy the former position of the peripheral protoplasmic ring. In consequence of this shrinkage the staining processes also are very much interfered with, the elements take the dye in a different manner, and the recognition of the cell types becomes a matter of no small difficulty.

With a more severe degree of shrinkage the bands of altered cytoplasm are prone to rupture, and on manipulation of the section, the cell drops out of its capsule leaving a clear open space. Such an appearance we have not yet seen as a result of a true degenerative process, and we hope to show that as the cell undergoes disintegration, its site is gradually filled up by proliferation of the surrounding connective tissue nuclei.

It seems to us therefore that unless *post-mortem* change

and artifical shrinkage are entirely eliminated, the existing true pathological processes are to a very large extent masked, and artefacts or pseudo-pathological processes receive an attention sufficiently great to lead to a grave source of fallacy in the estimation of the extent of the morbid change present.

## Morbid Changes in the Cells of the Posterior Root Ganglia in General Paralytics.

It has been necessary to enter into a lengthy description of the cell types in the normal posterior root ganglia, for the reason, that each type degenerates in a specific manner distinct from the others, and a knowledge of their normal structure is therefore necessary, in order to recognise each type at an early stage of degeneration, and to follow it through its progressive phases. This we have done in six typical cases of general paralysis, uncomplicated by tabes, only examining such ganglia as we were able to secure before *post-mortem* change had set in. In every case ganglia were taken from the cervical, dorsal and lumbar regions, and having been prepared according to the method recommended above, were stained by Lugaro's modification of Nissl's method. Toluidin blue being used in preference to thionin.

The chromatolysis revealed by this method must naturally be described under each of the five types of cells existing in the ganglia.

Of the two varieties of large, clear cells which are described as No. 1 and No. 2, the former persists practically unaltered, much more frequently than the latter. Chromatolysis is shown in the first type by a general breaking up of the granuliform elements throughout the cell, and by an early peripheral displacement of the nucleus. The elements around the nucleus often show a tendency to preserve their shape for a considerable time after those in the other parts of the cell have disintegrated. A cell in an advanced stage of degeneration shows its altered chromophile elements in the form of a fine dust scattered throughout the cell body (fig. 7).

The second type of cell, though structurally somewhat closely resembling the first type, is easily identified owing to the characteristic peripheral chromophile band which persists to a very late period of degeneration. The seat of the primary stage of degeneration is much more local than in the preceding type.

It will be remembered that the centre of the cell body is occupied by a granuliform mass of elements, and it is at the periphery of this mass, that is, immediately internal to the peripheral chromophile ring, that we have observed the process to begin (fig. 2).

The disintegration proceeds progressively towards the nucleus, and at the same time the peripheral large chromophile elements are seen to become united by their extremities to form a complete ring around the cell (fig. 3). With the progression of the degeneration, the central granuliform mass gradually disappears, until in the later stages the cell is seen to possess a well-stained nucleus and a peripheral chromophile ring only, the two being separated by clear, unstained cytoplasm (fig. 4). Occasionally, when the chromatolysis has reached this stage, a small, diffuse, chromophile mass is seen attached to the nuclear wall (fig. 4), and when the nucleus is excentric, the mass is present only on the side of the nucleus which is turned towards the centre of the cell.

During the progress of the chromatolysis the nucleus may pass to the periphery of the cell, but very frequently it remains central or nearly so.

In the "scure" cells (type 3), with the onset of chromatolysis, the nucleus passes towards the periphery and the centre of the cell becomes clearer owing to the breaking up of the chromophile elements. The degeneration spreads until chromophile elements are recognisable only at the periphery, and the remainder of the cell stains diffusely blue.

The cells at this stage somewhat resemble the cells of type 2 in an advanced stage of degeneration, but they are much smaller in size, and do not stand out so clearly from surrounding structures, and the nucleus is much more

FIG. 9.

Note the cell in centre of the field. The nucleus is excentric and in its vicinity the chromophile elements are large. At the opposite end of the cell the chromophile material is broken up into fine granules. This is a degenerating No. 4. Zeiss, apochrom., obj. 8 mm., oc. 4.

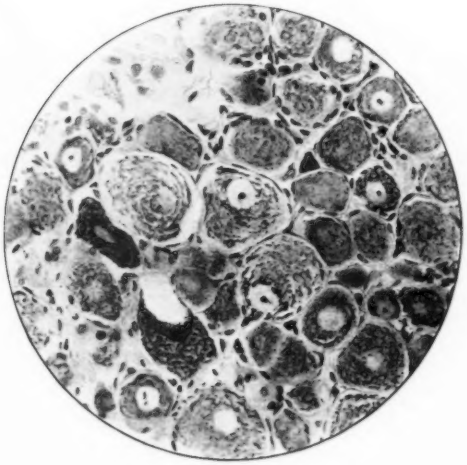

FIG. 10.

Two cells in centre of the field with elongated chromophile elements and excentric nucleus. Those are Lugaro's 5th type, and called by him "the corticose cell." Zeiss, apochrom., obj. 8 mm., oc. 4.

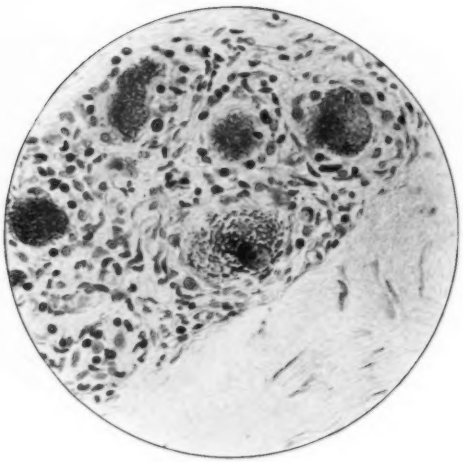

FIG. 11.

Note cell with excentric nucleus, attached to which there is a chromophile condensation which points towards the centre of the cell. At the opposite pole of the cell the chromophile elements are breaking up. This is a degenerating vorticose cell. Zeiss, apochrom., obj. 8 mm., oc. 4.

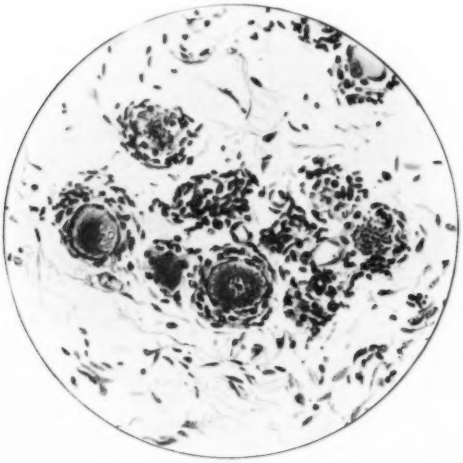

FIG. 12.

There are two degenerating cells around which can be seen a proliferation of nuclei. Above those two cells aggregations of nuclei are seen occupying the former site of degenerated nerve-cells. Zeiss, apochrom., obj. 8 mm., oc. 4.

frequently displaced to the periphery than in the large clear cells.

In type No. 4 the chromatolysis may commence at one focus in the cell, or may have a diffuse character from the beginning. The large elements are seen to become broken up into small, irregular granules, and the nucleus tends, at an early stage, to assume an excentric position, and when it has reached a point quite close to the periphery the largest remaining elements are observed in its immediate vicinity (fig. 9), while those in the other parts of the cell are represented by a fine diffusely staining dust.

This type of cell is always recognisable in its later phases of degeneration by the prominent, thick, chromophile elements placed between the sides of the excentric nucleus and the edge of the cell (fig. 9).

It has been difficult in the last type, that is the vorticose cell, to follow out the morbid changes, because of its comparative rarity. We have examined numerous sections from the ganglia of general paralytics, and from cases of acute insanity, and we have been struck by the scarcity of this type of cell. Dr. Eades, who is at present working at the changes in the posterior root ganglia of epileptics, confirms this observation, having himself noticed how infrequently this type of cell is met with. We have, however, discovered cells in various phases of degeneration, and in them we have noticed that the chromatolysis commences at the periphery by a breaking up of the elements, and at the same time there is frequently a large condensation of deep staining chromophile substance attached to the side of the nucleus which is turned towards the centre of the cell (fig. 11).

The nucleus maintains its peripheral position, and at its sides some slender, elongated elements remain practically uninjured. These elements are no longer seen in the other parts of the cell. The elements which do remain intact are never so thick or so prominent as those seen in the cells of type 4 at a similar stage of degeneration, so that an examination of the elements around the excentric nucleus will still reveal the type to which the cell belongs.

Although it has been possible to classify the stages of

chromatolysis of the various ganglion cells under the above-mentioned types, we have seen a few cells which have become so disintegrated as to be beyond such classification.

When cells reach a more advanced stage of degeneration than that described above, we have noticed that the surrounding connective tissue nuclei proliferate and form a dense ring around the cell residue, encroach upon it, and gradually fill up the site previously occupied by it (fig. 12). Such extensive forms of degeneration, with nuclear proliferation around, occur with great infrequency, and it is only around cells showing this advanced stage of disintegration that any degree of nuclear proliferation is found, and moreover, it progesses *pari passu* with the destruction of the cell, until finally there is only a group of proliferated nuclei left to indicate the position which the ganglion cell originally occupied (fig. 12).

Notwithstanding the fact that so many ganglion cells show a considerable degree of morbid change, yet it would be quite erroneous to assume that those cells were dead, seeing that their nuclei not only maintain their regular outline, but also show a normal affinity for the staining reagent. Such being the case, we regard them as still capable of regeneration, a fact which is borne out by the experimental work of Lugaro and others.

His work on the cells of the posterior root ganglia in the dog and rabbit after resection of the afferent nerve proves conclusively that, although the chromophile elements may almost entirely disappear, yet complete restoration is possible, and the normal appearance of the cell may be re-established on the completion of the process of repair.

In our sections we have frequently noticed appearances which suggest an attempt at regeneration of the chromophile material taking place in the cell.

When the breaking up of the chromophile elements has reached its height, we have found not infrequently a small chromophile mass attached to the outer side of the nuclear wall which looks towards the centre of the cell, and in examples which may be taken to show more advanced stages of regeneration, this mass may reach a considerable

volume, occupying a large part of the centre of the cell, and Lugaro has shown that it is from this chromophile mass that the new Nissl-bodies are formed by diffusion and reconstruction of the chromophile granules.

Such appearances, coupled with the fact that the nucleus of the nerve cells invariably remains well stained, and persists in an apparently healthy condition until the latest stages of chromatolysis seems to explain to us why there are so many cells found showing the various stages of degeneration which we have described, and why there are so few cells which go on to complete destruction.

Granted that the nucleus does not die, then regeneration is possible on the removal of the cause of the morbid change; and it can hardly be doubted that the cause in this instance is the presence of toxines, which are now admitted by all to be present in the blood of general paralytics.

But it is conceivable that the toxicity which affects the tissues in this disease, is not constant in its intensity, but is liable to waves of remission or intermission during which the affected tissues, if not too severely injured, can recover, and this fact is borne out by clinical evidence.

It can easily be understood, then, how it is that we have found so few examples of the destruction of cells in the posterior root ganglia of general paralytics, and we believe that the cells of this system become affected by the action of toxines upon them, but that on the removal of those toxines, the cells are capable of regeneration, and that probably they may react to the poisonous effects of those toxines and become repaired more than once in the course of the disease, before their resistive power is finally overcome, and they undergo complete destruction.

We have shown that many cells become chromatolysed in consequence of the action of toxines upon them, but the chromatolysis stops short of actual destruction of the cell, leaving the nucleus apparently unimplicated. Recovery being still possible, it can readily be understood that the central prolongation of those cells ought not to undergo a secondary degeneration; and as a matter of fact repeated examinations show that they do not. The posterior nerve

roots examined by the Marchi and Weigert-Pal methods, even in teased preparations, present a very slight degree of degenerative change, and this is not to be wondered at, when one considers how few ganglion cells show extreme phases of chromatolysis such as would lead one to suppose that they were dead.

In this connection one cannot help noticing how frequently one finds an amount of fibre degeneration in the posterior columns of the cord, which cannot be accounted for by the degree of degenerative change in the posterior root ganglia. We acknowledge that here we are at variance with Sibelius and Vyrubow, who affirm that the degeneration in the posterior columns depends on the destruction of the posterior root ganglion cells. A glance at their description of the alleged morbid appliances reveals the fallacies contained therein, as they base their conclusions on such descriptions as a granuliform degeneration of the chromophile elements—although as we have pointed out a granuliform condition of the chromophile elements is a normal feature of types 1, 2, and 3—and a paucity of cells revealed by the fact that there are clear spaces in which no cell structure can be detected. Such pictures as the latter can never be accepted as indices of morbidity, as we have demonstrated that *post-mortem* change and faulty fixation can account for them entirely.

In addition to this, experience has shown us that as the cell goes on to complete destruction, its site becomes gradually occupied by proliferation of connective tissue nuclei. Even in acute insanities, where one finds a much more rapid form of chromatolysis in certain cells, although the chromophile substance may be wanting almost throughout the entire cell, yet the cell retains its normal shape and preserves its proper relationship with the surrounding structures.

As we have indicated before, spaces and shrinkage are artefacts, and if discounted from Sibelius and Vyrubow's work, the amount of fibre degeneration will assume a preponderance greatly in excess of the true degenerative change in the ganglia, and the results of those authors' research will more nearly approximate to those found by us.

We are not alone in considering that the changes in the posterior root ganglia are insufficient to account for the changes in the posterior columns, as Campbell and Fürstner have found little abnormality in the ganglion cells beyond a tendency to hyperpigmentation. Rubaud supports the above view, and considers that the scattered degeneration of the posterior columns occurs secondarily to an affection of the cells in Clarke's column. It seems to us more likely, however, that the diffuse degeneration found in the posterior columns in general paralysis uncomplicated by true tabes, is due to the toxines in the circulation which are capable of attacking the fibres everywhere in their course throughout the cord.

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# ON THE CHANGES IN THE NERVOUS SYSTEM IN A CASE OF OLD-STANDING AMPUTATION.

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## HISTORICAL.

FOLLOWING amputation of a limb, hemiatrophy of the spinal cord was observed by Bérard[1] in 1829. Krause and Friedländer[2] found that both gray and white matter in the spinal cord underwent atrophy on the same side as the amputation. Vulpian, Dejerine-Mayor, Hayem-Gilbert, Edinger, Gudden, Erlitzky, Homén and Vanlair confirmed this statement as regards the gray matter. Vulpian[3] noticed atrophy of the posterior horn alone on the side of amputation; Hayem-Genzmer and also Vanlair[4] found the anterior horn alone affected; while Hayem-Gilbert, Drechfeld, Edinger, Krause-Friedländer, Homén[5] and Bignani and Guanieri[6] state that both anterior and posterior horns are affected.

Varying statements are made as to the condition of the cell-groups in the anterior horns on the side of amputation (or nerve division). Thus Dejerine-Mayor[7] state that the antero-internal group exhibit a defect in number of cells; Drechfeld, Hayem-Gilbert,[8] and Homén on the other hand,

[1] *Bulletin de la Société Anatomique.*
[2] "Ueber Veränderungen der Nerven und des Rückenmarkes nach Amputationen." *Fortschritte der Medicin*, 1886, S. 749.
[3] *Archives de physiol. norm. et pathologique*, 1868, I., p. 443; 1869, II., p. 675.
[4] "Des altérations nerveuses centripètes consécutives à la section des nerfs, etc." *Académie Royale de Médecine de Belgique*, 1891.
[5] "Veränderungen des Nervensystems nach Amputation." *Beiträge zur pathologischen Anatomie von Ziegler*, 1890, S. 304.
[6] *Bolletino della R. Academia di Roma*, 1888.
[7] *Bulletin de la Société de Biologie*, 1878.
[8] *Archives de physiol. norm. et path.*, 1884, III., p. 430.

find that the postero-lateral group is chiefly but not exclusively affected; while Krause and Friedländer find that the postero-lateral group is alone affected. According to the last two observers, and also Homén, Clarke's column is affected as well.

By Hayem-Gilbert a diminution in size of the nerve-cells of the spinal cord is described; Genzmer, Krause-Friedländer and Dejerine-Mayor state that a diminution occurs in the number of the cells, while Erlitzky, Drechfeld and Homén find that both processes occur together after amputation. The spinal ganglion cell-bodies persist for some time after peripheral or distal fibres have degenerated (Friedländer and Krause, Homén, Vanlair, Marinesco).

Pelizzi[1] describes degenerative changes in the cord after amputation.

Having thus noted the types of change which have been described it will be well to briefly review the alterations which more recent investigators have found in individual cases.

Marinesco[2] examined three cases:—

(1) Male; amputation of middle of left thigh at 30. Death at 51 from dementia paralytica following an attack of apoplexy. Asymmetry of cord, left side smaller in lumbo-sacral region. The cells of the postero-lateral group in the anterior horn are only one-third of the number on the opposite side. Elsewhere a lesser degree of disappearance of cells on this side. Slight diminution in number of cells in left postero-lateral group in the cervical region. Little change in dorsal region.

(2) Male; amputation of middle of right upper arm at 40: death at 50. Atrophy of right side of cord in cervical region. Anterior and posterior nerve-roots atrophied (especially the latter). Diminution of the number of cells in the right lateral horn and also in the other cell-groups in the cervical region.

(3) Age at death and date of amputation [of left thigh] unknown. In the lumbar region a left-sided atrophy of the cord, not so marked as in the first case. No distinct change in the number of the anterior horn cells on the affected side. The cells

[1] "Sur les modifications qui surviennent dans la moelle epinière des amputés." *Arch. ital. de Biologie.* Tome xviii., I.

[2] "Ueber Veränderung der Nerven und des Rückenmarks nach Amputationen; ein Beitrag zur Nerventrophik." *Neurol. Centralbl.* B. xi., SS. 463-467; 505-508; 564-574, 1892.

of the posterior root-ganglia on the affected side appear intact. The neuroglia showed no hyperplasia.

Gregoriew[1] describes in detail the state of the spinal cord in five cases of amputation, two of upper limb, two of the thigh, and one of the leg. In four cases changes were found in the spinal cord; in one case of amputation of the thigh one year previous to death, the spinal cord appeared perfectly normal. The alteration observed consisted in atrophy of the elements of the cord on the side of amputation. The earliest parts affected were the posterior roots and columns. Later the motor portion of the cord was also affected and the intensity of the change depended upon the length of time elapsing since the amputation. The statement that the postero-lateral cell-group in the anterior horn was especially affected Gregoriew could not confirm; he found the ventral and lateral groups much more affected. In two cases degeneration of the posterior roots, slight in degree was observed, and in one case the peripheral nerves showed true degeneration and not mere atrophy.

Sibelius,[2] in a man 70 years of age dying from pneumonia, in whom five years before death the left lower extremity was amputated just above the knee-joint found that the anterior horn-cells in the lumbar enlargement of the cord were fewer in number on the side of amputation than on the opposite side. This diminution in number affected chiefly the postero-lateral group, but the other cell-groups were also affected. The changes in the anterior nerve-roots were unimportant, being considerably less striking than those in the posterior roots. Some of the nerve-cells in the ganglia on the posterior roots had disappeared and others had atrophied, on the side of the amputation in the segments corresponding to the limb removed. In the left posterior column in the same region there was a distinct atrophy with rarefaction of the nerve-bundles, and the course of this atrophy corresponded in the cord to that of the posterior

[1] "Zur Kenntniss der Veränderungen des Rückenmarks beim Menschen nach Extremitäts-amputationen." *Zeitschr f. Heilk.* 1894, Bd. xv.

[2] "Till kännedomen om der efter amputationer uppkommande förändringrana i nervsystemet met special hänsyn till de spinokutana neuronerna." *Finska läkaresallsk handl.* 1897, xxxix., 10, S. 1379.

roots derived from the affected ganglia. The reflex collaterals were fewer in number on the side of the amputation than on the opposite side. The cells in Clarke's column were also diminished in number on the side of the amputation. Sibelius regards the changes in the posterior columns, posterior roots and spinal ganglia as consisting of a degeneration of the spino-cutaneous neurons as a result of injury to their axis-cylinders in the peripheral nerves, in addition to which the trophic ganglia of these cells in the spinal cord also degenerate.

Elzholz[1] found in the stump of the limb after amputation several years previously [two cases were studied] that the large medullated fibres in the divided nerves became diminished in size as they descended in the stump, the diminution being due solely to thinning of the myelin sheaths, while at the same time a progressive diminution in number both of large and small medullated nerves took place. Non-medullated nerve-fibres made their appearance in increasing numbers as the extremities of the divided nerves were approached, these arising to all appearance out of the small medullated nerves.

The following is a summary of the changes, resulting from amputation of a limb, which the observers already quoted have noted :—

In the first place comes hemiatrophy of the spinal cord on the side of, and in the segments corresponding to, the lesion. A single exception is found in one of Gregoriew's cases, but as amputation occurred only one year prior to death it is probable that this change in the spinal cord had not had time to become manifest. The hemiatrophy affects both white and gray matter. In the white matter the nerve-fibres are atrophied and true sclerosis results.

Beyond this point there is difference among the observers quoted. Sometimes the posterior horn, sometimes the anterior horn, sometimes both together, have been found affected ; the nerve-cells have been found simply atrophied in some cases, while in other cases they have been found

[1] "Zur Histolgie alter Nervenstümpfe in Amputirten Gliedern." *Jahrbücher f. Psych.* Bd. xix. Compare Marinesco, *loc. cit.*

diminished in number on the side of amputation; in some cases the defect of cells has affected chiefly the antero-internal, in others the postero-lateral cell-groups of the anterior horn, while defect of Clarke's column has also been observed on the side of the injury. An exception to the usual diminution in number of the anterior horn-cells is found in Marinesco's third case.

The defect in the white matter has been noted to affect the posterior column corresponding to the side of amputation (Gregoriew, Sibelius and others), but the defect is not confined to this situation.

In animals amputation is followed by spinal cord changes similar to those occurring in man. These are more pronounced in developing than in adult animals.

The posterior roots at the level of the amputation are atrophied. True degeneration has also been described.

The ganglia on the posterior roots have, in different cases (1) appeared intact, or (2) presented both atrophy and defect of nerve-cells.

Degeneration has been met with in the peripheral nerves after amputation. Simple atrophy has usually been noted.

Little attention has been paid to the condition of the brain following upon amputation.

It is obvious from the foregoing that much further study of the changes in the spinal cord, posterior root ganglia, spinal nerve-roots and peripheral nerves in a larger series of cases is required before any very precise statement can be made of the extent and distribution in different cases of the structural alterations in the nervous system resulting from amputation, and the apparent discordance in the changes met with up to the present reconciled. Such observations are of very great importance in so far as they are likely to increase our knowledge, on the one hand, of the relation of the segments of the spinal cord to body areas and, on the other hand, of the connections and interdependence of the various neurones of the spinal axis.

It is very desirable that the condition of the brain after amputation should be also recorded. An examination limited to the spinal axis loses much of the value which it would otherwise have.

The case which forms the subject of the present investigation appears peculiarly fitted for the observation of some of the above points owing to the long period of time elapsing between amputation and death, and the excellent physical health and the very active life led by the patient up to within four years of death. On the other hand the condition of general brain atrophy accompanied by cortical softening in the left occipital lobe, which occurred towards the close of the patient's life, places a difficulty in the interpretation of some of the changes noted in the basal portions of the brain.

## History of Case.

Patient was a male, 61 years of age at the time of death, whose occupation had been that of a house-to-house hawker, doing a large business with a horse and cart. When 19 years of age his right upper limb was amputated at the middle of the upper arm (fig. 1). Six years before his death he failed in business, became depressed, and after twice attempting suicide was admitted to the asylum. At the end of three months he was discharged. About a year after his discharge he suffered from influenza which left him irritable. Previous to this illness his general health had been good, and he had been for twenty years a total abstainer. Subsequently he deteriorated mentally and physically. His memory failed and he became demented. He was re-admitted to the asylum twenty-one months before death.

At the time of death there was a fairly extensive range of passive movement at the right shoulder-joint. The muscles of this shoulder were wasted to an extreme degree (fig. 1; note in particular the condition of the deltoid and pectoralis major), so that the head of the humerus and the rest of the bony skeleton of the shoulder were readily recognisable on inspection and palpation. The muscles attached to the left shoulder were of good development. There was some atrophy of the right trapezius, but the sterno-mastoids were of nearly equal development.

## The Spinal Cord and Posterior Root Ganglia.

The spinal cord upon removal showed some degree of asymmetry in the cervical region and upon close examination right-sided atrophy was observed. This condition was, however, far more readily noted after hardening when transverse sections

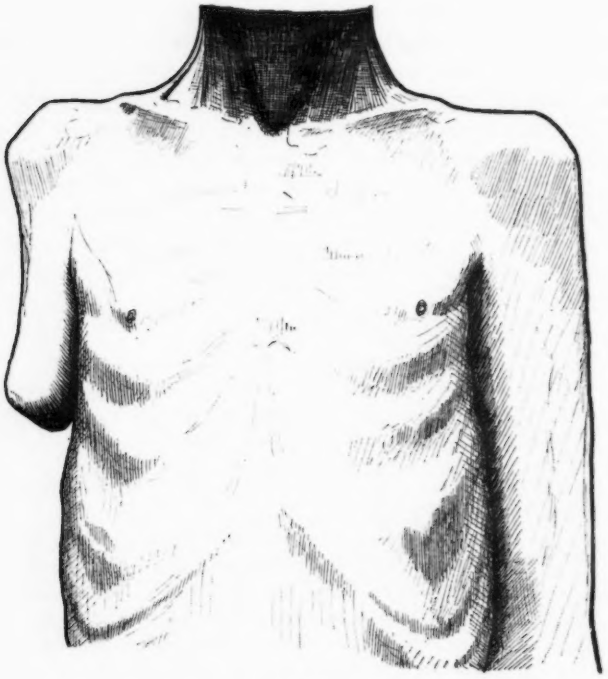

FIG. 1.

Sketch of the chest and the amputated right arm, together with the opposite upper limb, of the patient whose case is described in the text. The shoulder muscles on the right side are much atrophied, the contrast being very striking when comparison is made with the opposite shoulder. The right pectoralis major also is extremely wasted. The anterior edge of the trapezius is thin on the right side, but the sterno-mastoids are of equal size. The patient's general development is otherwise good.

were made.[1] Contrary to expectation there was no obtrusive difference in the aspect of the nerve-roots, posterior and anterior, on the two sides in the lower cervical and upper dorsal regions,

[1] The spinal cord after removal was hardened in alcohol. Subsequently each segment was sectioned transversely, the sections being stained by Nissl's method. In studying the condition of the nerve-cells as to size and number, numerous sections of each segment, made at varying levels of the segment, were examined and compared, it not being possible to draw reliable conclusions from the examination of single sections. Sections were also stained by v. Gieson's method, by carmine and by iron-hæmatoxylin.

The posterior root ganglia were examined by Nissl's and v. Gieson's methods.

but the anterior nerve-roots appeared on both sides somewhat small in this region.

*Hemiatrophy.*—The right-sided atrophy of the spinal cord (fig. 2) was strongly marked in the second to the sixth cervical segments, less marked in the next two cervical segments, slight in the first and second dorsal segments, and indistinct below the latter level. It affected both white and gray matter.

*Posterior columns.*—There was some wasting of the right posterior column in all the cervical and the first dorsal segments. Below the first dorsal segment the inequality disappeared. No marked sclerosis was, however, recognisable in the posterior columns. The position of the septum between the columns of Goll and Burdach was not sufficiently well defined to allow a positive statement to be made as to the existence of a localised atrophy in the right upper limb area of the former.

*Antero-lateral columns.* — The right antero-lateral column was smaller than the left. The wasting was noticeable in the cervical region and could be traced in the dorsal cord to the tenth segment, gradually diminishing in degree. The atrophy appeared to be largely in the situation of the crossed pyramidal tract (fig. 2) and was accompanied by an increase in the nuclei and staining capacity by Nissl's method of this area. Weigert's stain showed an increase of neuroglia fibrils. There was a similar sclerosis, much slighter in degree in the same situation on the left side, extending as low as the eighth dorsal segment The right antero-lateral column did not appear to be affected except in the situation of the crossed pyramidal tract. The portion of the right antero-lateral column lying between the anterior horn and the median septum is slightly narrower than its fellow in the cervical region. This difference disappears below the cervical region. The large size of the fibres of the direct cerebellar tracts permitted these columns to be recognised; no change was found on the right side in the amputation segments. The same held good of the antero-lateral ascending and descending cerebellar tracts.

*Gray matter. Extent.*—The gray matter of the right anterior horn was atrophied throughout the cervical, and in the first dorsal, segments. Below the first dorsal segment no well defined difference is recognisable. The right posterior horn was not apparently wasted. It was shorter and thicker than its fellow, but its superficial area in section was about equal to that of the opposite horn (fig. 2).

*Anterior horn-cells.*—The large multipolar cells in the anterior

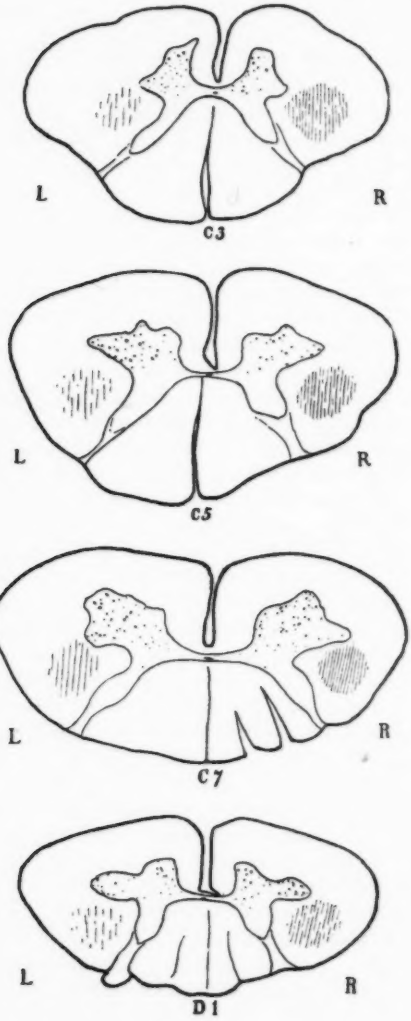


FIG. 2.

Outline sketches of transverse sections of the the third, fifth and seventh cervical, and the first dorsal, segments of the spinal cord, all drawn to the same scale, the large multipolar nerve-cells in the anterior cornua being also

indicated in respect of size and number. There is hemiatrophy of the cord on the right side, both gray and white matter being defective. The diminution in size of the gray matter affects the anterior cornu, but not the posterior cornu to any marked extent. The large multipolar nerve-cells of the anterior cornu are also deficient on the right side, the defect in C 5 and C 7 being marked in the outer part of the anterior horn, and affecting both the size and number of the cells. Sclerosis of the right crossed pyramid tract is indicated by shading. A slighter degree of sclerosis is found in the left crossed pyramidal tract. R, right side; L, left side, in this and the succeeding figures; stained by Nissl's method. *Magnified five diameters.*

horn were diminished both in number and size on the right side. When a large number of sections from each segment are examined this diminution was found in the fifth, sixth, seventh and eighth cervical, and to a slight degree in the first dorsal, segments.[1] This change was chiefly noticeable in the outer part of the anterior horn; the antero-internal cell-groups were more slightly if at all affected. Above the fifth cervical, and below the first dorsal segments, no constant difference on the two sides was recognisable; in the lumbar and sacral segments the cells on the two sides were equal. It is difficult to form a quantitative estimate of the difference on the two sides in the affected segments by counting the nerve-cells, owing to the difficulty of making a sharp separation between large and medium sized cells. I give, however, the following estimate of the relative number of multipolar anterior horn-cells on the two sides, obtained by counting as accurately as possible the number of these cells in forty successive sections from the eighth cervical segments, each 25 $\mu$ thick, those on the left side being taken at 100 for the sake of comparison. (The actual number counted on this side was 3,450.) The figures thus obtained, which must be regarded as only approximately correct, were: Right side, large 6, medium 77, together 83; left side, large 16, medium 84, together 100.

*Posterior horns.*—The cells in the right posterior horn showed no marked difference in number and size from those in the left posterior horn.

In consequence of the atrophy of the right anterior horn and the defect of white matter the spinal cord appears distorted on transverse section, and the anterior and posterior median septa tend to curve over to the right side in front and behind (fig. 2).

*Sheath and blood-vessels.*—At the necropsy the pia-arachnoid was found to be whitened and there was much cerebro-spinal

[1] In examining transverse sections note is taken only of such change in number and size of multipolar anterior horn-cells as predominates in a series of sections of the same segment. Individual sections are not necessarily representative of the general condition of the segment in respect of its anterior horn cells.

fluid about the cord. On section the pia-arachnoid was seen to be thickened. The blood-vessels were thick-walled in the situation of the anterior septum. No change was noted elsewhere. The dura mater was unaltered in aspect.

*Nerve-roots.*—As already stated no marked one-sided defect in the size of the posterior or anterior nerve-roots was noted, though the latter seemed somewhat scanty on both sides at the cervico-dorsal junction. Nor were the root-fibres obviously of smaller diameter on the right side in the cervico-dorsal region.

*Posterior root ganglia.*—The posterior root ganglia could not be recognised to be smaller on the right side than on the left in the cervico-dorsal region. It is, however, difficult to observe a small alteration in their size accurately owing, on the one hand, to the adhesion of these ganglia to the dura matral sheaths requiring some dissection in order to expose the ganglia and, on the other hand, owing to the intermixture of nerve-cells and fibres. Microscopical examination also failed to reveal any constant or obtrusive difference on the two sides. The nerve-cells were of varying size consisting of large cells 78 $\mu$ to 50 $\mu$ in diameter, and smaller cells 35 $\mu$ to 25 $\mu$ in diameter, the former being relatively more and the latter relatively less numerous in the lower cervical and upper dorsal region than in the dorsal region below the upper two segments. The arrangement of chromophile material in the cell-bodies was unaltered on the right side, nor was the connective tissue increased. The appearance in transverse section of the mixed spinal nerves immediately beyond the ganglia was not markedly different on the right side from that on the left. No examination was made of the condition of the divided ends of the nerves in the stump.

## The Brain.

In considering the condition of the brain it will be convenient to note first of all the general appearance of the brain mantle and its coverings and then to study the changes present in the basal portion of the encephalon as exhibited in a series of transverse sections from below upwards.

*Cerebrum.*—The first point to note is the condition of senile atrophy which the brain (1,128 grammes) presented. The brain mantle was wasted generally, especially in the parietal and frontal regions, and corresponding to this wasting there was widening of the sulci and fluid in the meshes of the pia-arachnoid. The latter membrane was white and opaque at the vertex and to a less extent

at the base where the cisterna magna and pontis contained much fluid. The ventricles were of large size, the left lateral ventricle being larger than its fellow (fig. 5). The ependyma was everywhere smooth. The choroid plexuses of the lateral ventricles were larger than normal.

There was old softening on the left side involving the apex of the cuneus and the adjoining part of the lingual convolution, extending to the ependyma of the lateral ventricle and reaching posteriorly to the optic radiation. With this exception focal lesions were absent from the cerebrum. The dura mater was adherent to the skull-cap and presented two calcified plaques, in the falx-cerebri, the larger being four centimetres long and the other slightly smaller; on the inner surface of the dura a thin

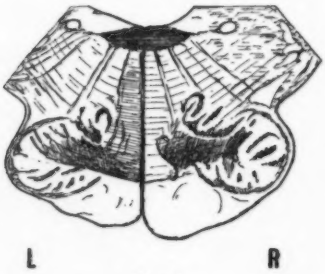


FIG. 3.

Transverse section of the medulla oblongata through the middle of the olivary bodies. On the left side the anterior pyramid is much smaller than on the right. The olivary bodies are of nearly equal size. The superior pyramidal decussation presents a slight inequality on the two sides, there being more decussating fibres on the left side of the median raphe than on the right. *Magnified three diameters.*

rusty pellicle was present opposite the right temple and in the middle fossa. The basal vessels were generally thickened and stiff but presented very little nodular atheroma.

*Medulla oblongata.*—Turning now to the structures at the base of the brain, the medulla oblongata comes first for consideration (fig. 3). The left anterior pyramid was much wasted as compared with its fellow. This change was very striking. The left half of the section was smaller than the right, the difference being distinct though slight even in the dorsal region of the medulla. The olivary bodies were of nearly equal size. The superior pyramidal decussation was not symmetrical; more decussating fibres were seen on the left side of the median raphe than on the right. The

hypoglossal and vagal nuclei were equal on the two sides, and the posterior column nuclei were also of nearly equal size.

*Pons and cerebellum.*—In the pons Varolii the same left-sided atrophy involving the pyramidal bundles, which here are of larger size than in the medulla oblongata, was observed (fig. 4). In the dorsal region of the pons there appeared to be little diminution of size, but the two halves of the section were not perfectly symmetrical; this want of symmetry did not appear to be wholly due to an obliquity in the plane of the section. The posterior longitudinal bundles were of equal size. There was a difference in the

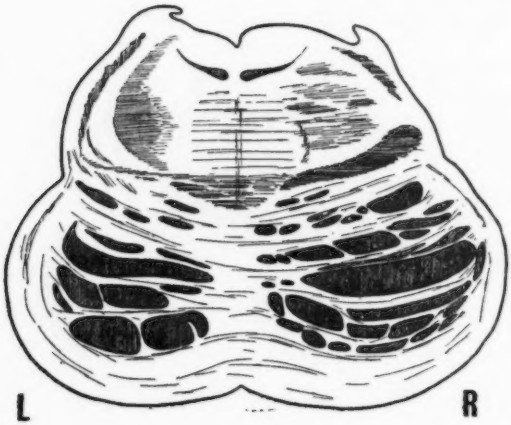


FIG. 4.

Transverse section of the upper part of the pons Varolii. The section is slightly smaller on the left side than on the right, owing to diminution in size of the pyramidal bundles. The dorsal portion of the pons does not exhibit a similar asymmetry. The fibres of the fillet are not cut quite at the same level on the two sides. *Magnified three diameters.*

appearance of the fillet on the two sides apparently due to a difference in level (fig. 4). The cerebellum presented no change calling for note; the dentate nuclei were equal on the two sides.

*Mesencephalon.*—In the mesencephalon there was distinct atrophy of the pes pedunculi but the tegmentum was nearly equal in the two halves of the section.

*Basal ganglia.*—Both optic thalami were of small size (fig. 5). The left was however of much smaller size than the right, a difference which was much greater, when the thalami were viewed

from behind, than would appear from fig. 5. This left-sided wasting affected especially the ventral portion of the thalamus and the pulvinar but the anterior and dorsal portions also suffered in a lesser degree. The corpora geniculata and optic tracts showed no marked one-sided wasting.

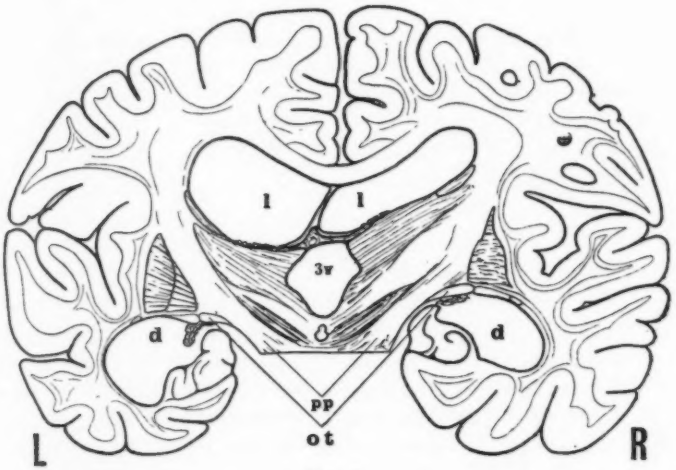


FIG. 5.

Frontal section of brain a short distance behind the corpora mammillaria. The sulci are widened and the lateral ventricles, *l l*, their descending horns, *d d*, and the third ventricle, 3 *v*, are dilated. The optic thalami lying on each side of the third ventricle are flattened. The left thalamus is smaller than its fellow, being wasted below in the subthalamic region. Below the thalami, there is seen on each side the locus niger, and externally and below this, the pes pedunculi, *p p*, is seen. More externally the lenticular nuclei are seen, and still more externally the islands of Reil; *o t*, optic tracts, external to which the inferior pedicle of the optic thalamus and the tail of the caudate nucleus are seen on each side forming the roof of the descending horns of the lateral ventricles. The opening seen below the third ventricle is the end of the posterior perforated space. *Slightly reduced in size.*

The corpora striata were of fair size and nearly equal, the left being slightly the smaller.

The internal capsule on the left side was not smaller than its fellow in the situation of the fibres going to the right upper limb.

There was a marked difference in the aspect of the optic radiation and inferior longitudinal bundles on the two sides, the left being rather less than half the thickness from side to side of the right.

The microscopical examination of the brain added little further information. In the medulla oblongata the right cuneate and gracile nuclei were not markedly different from the left. In the mesencephalon sclerosis could not be demonstrated in the left pes pedunculi. The left hand and forearm areas of the cortex, were not different from the corresponding areas of the right cerebral hemisphere.

The thoracic and abdominal viscera call for little remark. The kidneys show marked interstitial nephritis. There was pulmonary emphysema and congestion. The heart muscle was friable, and the mitral and aortic valves thickened. The body was somewhat emaciated, and the muscular condition was poor, but except in the region of the right shoulder, no unilateral wasting was found.

## Review.

The more important of the changes in the nervous system noted in the foregoing may now be recapitulated and at the same time some observations offered on their significance.

It may reasonably be suggested that the failure to discover any marked degree of atrophy of the posterior root ganglia corresponding to the portion of the right upper limb removed is to be explained by the difficulty of investigating the condition of these ganglia, the nerve-cells lying among abundant nerve-fibres and the ganglion being surrounded by stout connective tissue, so that a limited degree of atrophy may readily escape notice. The non-appearance of any marked diminution in size of the posterior roots corresponding to the four lower cervical and the first dorsal ganglia, comparison of which is much more readily made, cannot however be explained so easily. According to the few observations made upon this point, a disuse atrophy and disappearance of spino-cutaneous neurons is the usual consequence of amputation, but it does not appear that this event always occurs to a degree sufficiently marked to be with certainty recognisable. No such change, for example, was noted in Marinesco's third case;[1] and the observations of Elzholz[2] suggest that the posterior root ganglion

[1] *Loc. cit.* [2] *Loc. cit.*

cells, which as Dogiel[3] points out are not all spino-peripheral, are capable of preserving their integrity to a greater extent than might at first sight be expected. Having regard to these considerations, it seems logical to infer that in the present case atrophy of spino-peripheral neurons really existed, but in too limited a degree to be recognisable by the methods of investigation pursued. It is probable that the results of amputation in the human subject vary in degree in different cases. In the present instance the patient led a very active existence, and the tendency to degenerative changes may naturally be supposed to be less than in those cases in which an inactive existence followed amputation. It is to be noted also that no diminution, recognisable on inspection, in the size of the anterior nerve-roots in the cervico-dorsal region occurred on the right side, though the anterior horn cells exhibited a distinct diminution in size and number. Nor were the anterior nerve-roots diminished in diameter to any noticeable extent in the right cervico-dorsal region.

Examination of the spinal cord is more readily made and is much more precise owing to the fact that here the two halves are placed side by side enclosed in a common connective tissue sheath. For this reason slighter degrees of atrophy are recognisable than is possible in the case of nerve-roots and posterior root ganglia. In the latter it is not possible to obtain with certainty sections of different ganglia at the same relative level, which are alone strictly comparable; and again atrophy of the ganglion-cells is recognisable only if considerable in degree and distribution.

The right hemiatrophy of the spinal cord in the case under discussion (fig. 2) affected the segments corresponding to the amputated limb, namely the fourth cervical to the first dorsal. It was not however confined to them, but involved also the remaining cervical segments, though not extending to the dorsal segments below the second. The hemiatrophy did not correspond in degree to the extent which the relation of the spinal segments to body areas would suggest. Thus

[3] *Anat. Anzeiger* xii., p. 140, 1896. Also *Internat. Journ. of Anat. and Physiol.* xiv., p. 73, 1897; and xv., p. 345, 1898.

the eighth cervical and first dorsal segments were less affected than the segments immediately above. It seems clear that in passing from the lower to the upper segments of the cervico-dorsal region, the hemiatrophy becomes increasingly representative of the segments of lower level. This at once raises the question, which of the constituents of the spinal cord are chiefly involved in the hemiatrophy?

Taking first the gray matter, the atrophy here it will be noted corresponded to the amputation segments but also involved the cervical segments immediately above. The atrophy appeared to be confined to the anterior horn, not involving the posterior horn. The diminution in size and number of the anterior horn cells corresponded closely to the segments supplying the portion of limb removed and it did not extend beyond these limits (fig. 2).

As regards the white matter, the right posterior column showed atrophy in the cervical region, but no sclerosis was recognisable, and it was not possible to determine to what extent the upper limb fibres were involved. In the antero-lateral region sclerosis was recognisable in the situation of the right crossed pyramidal tract, and to a less extent in the left crossed pyramidal tract (fig. 2).

At this point it will be convenient to defer further consideration of the state of the white matter of the spinal cord until some features in the condition of the brain have been referred to.

The hemiatrophy present throughout the cervical region of the cord was seen again in the medulla oblongata (fig. 3), pons Varolii (fig. 4) and mesencephalon, and in these regions the side of hemiatrophy was changed from right to left, and was clearly due principally to atrophy of the left pyramidal tract. This was especially noticeable in the medulla oblongata where each pyramidal tract is concentrated into a single bundle. In a horizontal section of the internal capsules no difference was noted between the two sides; there was no recognisable narrowing in the situation of the upper limb fibres. In the hand and forearm areas of the cerebral cortex no marked difference was recognisable between the two hemispheres. Nevertheless, in the light of our present

knowledge, the diminution in size of the left pyramidal tracts in the medulla oblongata, pons and mesencephalon must be attributed to atrophy of the corresponding cortico-spinal neurons, and perhaps of thalamo-spinal neurons also. And a similar explanation holds good in respect of the slighter sclerosis seen in the left crossed pyramidal tract of the spinal cord.

In the spinal cord again, as already mentioned, the right anterior horn in the upper limb segments was atrophied, some of the cells having disappeared or become reduced in size. It follows, therefore, that there was present in the case under consideration atrophy of two sets of motor neurons of different orders connected with the right upper limb: namely, cortico-spinal passing from the "motor" region of the cerebral cortex to the affected segments of the spinal cord; and spinal-peripheral connected with the muscle-innervation of the same region. The upper set of neurons corresponding to the opposite upper limb were also affected in a much slighter degree.

The question now arises, was this degeneration of neurons conditioned by the amputation? In the case of the lower set of neurons the distribution of the diminution in size and number of the right anterior horn cells in the segments of the cord appears to admit of no doubt that these changes were causally related to the amputation. Some doubt may, however, be felt as to whether the degeneration of the upper neurons was determined by the amputation, for the brain mantle had undergone senile atrophy. The marked wasting of the left anterior pyramid (fig. 3) is, however, strongly in favour of the view that the wasting of the left upper neurons was determined by the removal of the limb. Upon this point further observations in cases of old standing amputation will be of interest.

A reference to fig. 2 suggests that the hemiatrophy of the spinal cord is, as far as concerns the white matter of the antero-lateral column, largely due to atrophy in the situation of the right crossed pyramidal tract; at any rate such an explanation would account for the diminution in breadth of the right half of the spinal cord in the cervical region. Such

an hypothesis could only be settled by the occurrence of a lesion which would define the crossed pyramidal tracts, such for example as a total transverse division of the spinal cord. In the absence of this, the exact effect of the sclerosis of the right pyramidal tract in respect of the altered form of the cord cannot be stated.

The condition of the direct pyramidal tracts is similarly difficult to determine in the absence of a lesion causing descending degeneration of these columns. There was little difference in the width of the anterior columns in the cervical region, but some asymmetry was present.

The direct cerebellar tracts which could be recognised by the large size of their fibres, were unaffected in the cervical region. The same is true of the antero-lateral ascending and descending cerebellar tracts.

The condition of the sensory path requires further consideration. The posterior column nuclei in the medulla oblongata showed no marked change in aspect. There was present slight left-sided atrophy in the medulla, distinct from and additional to the atrophy affecting the anterior pyramid (fig. 3). There was also a difference in the aspect of the superior pyramidal decussation on the two sides, the significance of which is not clear. In the pons Varolii and the mesencephalon there was no clear evidence of hemi-atrophy dorsal to the pyramidal tracts.

The left optic thalamus was much smaller than the right (fig. 5), the diminution in size affecting chiefly its ventral and posterior aspects but involving to a slight degree its anterior and upper portion also. This is presumably caused by the co-existing softening on the mesial aspect of the left occipital lobe, and does not appear to stand in any causal relation to the condition of the right upper extremity. The left optic radiation was conspicuously small. The co-existence of senile brain-atrophy places a difficulty in the way of determining the significance of changes in the basal regions of the brain. Further observations are required in old amputation cases in which this complication is absent.

# Reviews.

*Die Myasthenische Paralyse (Bulbärparalyse ohne anatomischen Befund).* Von Prof. Dr. H. OPPENHEIM in Berlin. Mit 4 Abbildungen im Text und 3 Tafeln. Verlag von S. Karger. Berlin 1901.

THIS monograph will be welcomed by all who are interested in myasthenia gravis for its author has materially added to our knowledge of the disease and has by his previous writings largely contributed to its recognition as a distinct clinical entity. The work includes an abstract of all the cases hitherto reported.

The opening chapter is devoted to an interesting historical sketch, in which the part played by various observers in defining the disease as we now know it, is reviewed. After reference to the nomenclature, an abstract is given of the reported cases which appear to be undoubted examples of the disease; these are divided into three groups. Firstly, cases examined both during life and *post mortem* in which there could be no doubt as to the diagnosis (twelve); secondly, cases examined during life and *post mortem* which were in all probability examples of the disease (six); thirdly, cases in which although there was no *post mortem*, the clinical symptoms were sufficiently characteristic to make the diagnosis almost a matter of certainty (forty-one).

A short sketch of the chief clinical features and mode of onset of the disease is followed by a detailed description of the symptomatology based upon an analysis of the foregoing cases.

Among other points it is interesting to note the frequency with which the external ocular muscles are first affected (fifteen of fifty-one cases). In referring to the prominence of the eyeballs which is occasionally present in myasthenia gravis, the author remarks that this condition is not always associated with, and cannot therefore always be explained by, the presence of paralysis of the external ocular muscles; and he points out that other symptoms suggestive of exophthalmic goitre or, at all events, of a "forme fruste" of that disease are sometimes present.

The frequency with which death results from an attack of asphyxia is illustrated by a reference in tabular form to the eighteen fatal cases, in all of which death was due to this cause. Oppenheim is of opinion that true muscular atrophy should not be included in the symptomatology of myasthenia gravis; he thinks that in those cases in which a marked degree of muscular atrophy or qualitative disturbances of the electrical excitability were present there was probably some other disease or complication to account for their presence.

In the chapter on ætiology the author attaches importance to the neuropathic diathesis which, he believes, plays an essential part in the pathology. With regard to the influence of infective diseases as a causative factor, he remarks upon the probability that in some cases at least the myasthenia gravis was in existence prior to the onset of the infective disease, and its symptoms merely intensified by the acute intercurrent malady.

He points out that a thorough and detailed criticism of those cases in which pathological changes were met with in the nervous system fails to produce evidence of an organic lesion to account for the symptoms. The small hæmorrhages which have often been described in the central gray matter were, he thinks, probably produced during the death agony. He emphasises the occurrence in a few cases of congenital defects in the nervous system or other parts of the body as possibly throwing some light on the nature of the process. He suggests from a consideration of the pathological lesions which have been found in the other organs that here there exists a possible source for the production of a toxin. In common with the majority of writers Oppenheim regards the motor nerve nuclei or the whole of the corresponding motor neurons down to the muscles as the most probable seat of the lesion; while he classes the disease as a neurosis, dependent it may be to some extent on an associated congenital factor.

Before referring to the question of diagnosis an abstract of another series of cases is given. This fourth group includes the uncertain, doubtful, impure and mixed cases; these are considered separately either because of the existence of unusual symptoms or because the records are too imperfect to allow of certain classification.

The diagnosis is very fully treated of. It is pointed out that no single symptom is pathognomonic, but that the diagnosis must be based on the whole clinical picture and course of the disease.

Special attention is given to the differential diagnosis, and

tables are inserted showing the chief points of distinction between myasthenia gravis, chronic progressive and acute bulbar palsy. After an exhaustive consideration of the very close resemblance which exists between some cases of polioencephalomyelitis and myasthenia gravis the author comes to the conclusion that they are two distinct and distinguishable diseases.

Referring to prognosis, the absence of any undoubted recorded instance of complete and permanent recovery is remarked upon, and the gravity of the prognosis in those cases where pharyngeal and respiratory paralyses exist is pointed out.

Under the heading of treatment, in referring to the danger which accompanies the passage of the stomach tube, the suggestion is made that if it is considered necessary to pass the tube the throat should be previously cocainised.

Reference is made to the harmful effect of faradism, to the possible beneficial effects of galvanism, and to the uselessness of massage.

Although it cannot be said that any drug has been shown definitely to have a favourable influence on the course of the disease, mention is made of the various medicinal remedies which have been hitherto employed.

A very complete bibliography, not only on myasthenia gravis, but on all the papers referred to in the monograph, completes this valuable treatise.

It is much to be wished that all German authors would adopt the simple, clear style which characterises all Professor Oppenheim's works and makes them so attractive to his foreign readers.

EDWIN BRAMWELL.

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*The Nervous System and its Constituent Neurones.* By LEWELLYS F. BARKER, M.B.Tor., New York. (D. Appleton and Company, 1899, pp. 1084.)

THIS volume is stated in the title page to be designed for the use of practitioners of medicine and of students of medicine and psychology, and it is the outcome of a series of articles in the *New York Medical Journal.*

The book is divided into two parts. In the first 312 pages the newer conceptions of the histology of the central and peripheral nervous organs are reviewed, and in the second part the author states that "the attempt has been made to apply the neurone

conception—that is the cell doctrine—as consistently as possible in the explanation and description of the complex architectonics of the nervous system."

We are glad that throughout the work the word *neurone* is used to mean a cell belonging to the nervous system with all its parts and is not restricted to any particular part of the nervous unit.

It would be quite impossible to give a detailed account of this volume, and only a brief mention of its contents can be attempted.

The first part consists of five sections. In the first section on the history of the development of the neurone concept, after describing the old theory of Gerlach of the universal network, the researches of His, Golgi, Forel, and Ramon y Cajal are given, and the theory of the last named author that the axis cylinders end freely. The vital staining of Ehrlich and the study of degenerations by the Marchi and Nissl methods are well illustrated.

The question as to whether the terminals of the axone of one cell fuse with the dendrites of another cell is discussed, and Held's observations of this important point is well explained, and with regard to Apáthy's views the author thinks that the verdict "not proven" should be given.

In Section II. the external morphology of the neurones is dealt with, and the ingenious method of determining by polarization the age of the myelinization of the nerve-fibres is referred to. This section includes the description of the cell body and its dendrites, of the axones, collaterals, side fibrils, and interneuronal substance. The author thinks favourably of a recent view propounded by Nissl that there are probably fibrillar structures within the protoplasm of nerve-cells and also existing as extracellular nerve-fibrils in the gray matter, to which he attributes the highest functions of the nervous system, but the whole matter seems very hypothetical at present.

Section III. describes the internal morphology of neurones, and thanks to Nissl's method of staining, a new language has sprung up to designate the different behaviour to this reagent of normal and abnormal constituents of neurones. This section almost more than any other shows the vast strides which the minute study of nerve-cells has made in recent years and to the average neurologist who has not made a special study of the matter a glossary would be necessary to understand such terms as a "somatochrome nerve-cell of the arkyostichochrome variety in the apyknomorphous condition" if Dr. Barker did not describe all these changes in most lucid terms and smooth over the

difficulty of the words by giving the Greek derivations. In the last chapter of this section the author sums up in a comprehensive manner our present knowledge on the internal structure of the neurones.

Section IV. takes the histogenetic relation of neurones, describing the researches of His and others on the development of the spinal cord and medulla, of the peripheral nerves and the muscle masses. After thus taking the anatomy and histology of the neurone, we come, in Section V., to its physiology and pathology, and first to the metabolism and nutrition of the neurone, and then to its degeneration and regeneration. On the question of pathology the degenerations of Waller and Türck are described, but it is pointed out that, owing to improved methods of staining, the Wallerian degeneration theory will have to be modified, as it has been shown by various experiments that the nerve-cell is affected when its axone is divided, which is contrary to the doctrine of trophic centres formulated by Waller. The ablation experiments of van Gudden and Forel paved the way for this alteration in ideas, and Nissl is quoted as stating that changes in the cells of the facial nucleus can be detected as soon as twenty-four hours after the facial nerve has been divided.

Chapter XXI., in this section on the irritability of the neurones, is written in a highly philosophical spirit, and such subjects as the absence of complete repose of the neurones, as shown by the automatograph, and the dependence of muscular actions on the continuous passages of sensory impressions, as shown by Sherrington and Mott's experiments of dividing all the sensory nerves of a limb, are discussed, and also the "neurone threshold," or the degree of excitation of a neurone which just suffices to call forth a fruitful excitation, *i.e.*, a sensation or movement, in another neurone with which it is in contact. The author discusses the bearing of the neurone concept on Müller's doctrine of the specific energy of nerves, and gives it as his opinion—and one which seems most reasonable—that the constancy of the quality of the reaction, despite the variability of the external stimulus—as when the sensation of light is produced whenever the retina is stimulated—is due to the correlative differentiation of both the peripheral and the central organs, and not of one of these only.

In Chapter XXII., on the neurone as a unit of nervous function, the functions of the cell body and of its dendrites are discussed, and the original theory of Golgi, that the dendrites were purely for nutritional, and not for functional, purposes, is contested; and we think, with the author, that there can be

no doubt that the observations of Ramon y Cajal disprove this theory. On the question of the conduction in the neurones in Chapter XXIII., the author considers that it would be very unwise at present to state positively that nerve impulses may not pass in both directions in all neurones. The last two chapters of this section are on most interesting subjects, the relation of trophic to nervous functions in the neurone—where examination of nerve-cells in tired and normal animals shows an intimate relationship between states of nutrition of the cell and functional activity—and the histological alterations in neurones, due to action of poisons, compared with traumatism.

The rest of the work is taken up with "the grouping and chaining together of neurones in a complex nervous system like that of man and mammals." This is a minute description of the different tracts of the nervous system and their end stations, which have been found out by the methods of development or degeneration, and staining by various ways. The description begins with neurones connecting the sense organs of the body with the central nervous system; then the neurones within the central nervous system connecting the end stations of the axones of the peripheral centripetal neurones with other portions of the central nervous system, and goes on to the neurones directly connecting the central nervous system with the voluntary muscles of the body (lower motor neurones), and those which enter into conduction relation with the lower motor neurones and throw the latter under the influence of other centres (intermediary and upper motor neurones); and, lastly projection, commissural, and association neurones.

The author has not touched upon the structure of the sympathetic system, and as the work is devoted to histology and anatomical arrangement, no mention is made of the chemical side of neurology, with the exception of the tigroid matter in Chapter XII.

We have nothing but the highest praise for this work, and we congratulate Dr. Barker on the valuable contribution which he has made to neurology in America.

The book is not a mere compilation of facts, but on all doubtful points we have the advantage of Dr. Barker's opinion, which much enhances the value of the work. The references are exceedingly numerous, and no pains have been spared to give credit to the workers of all nations, and, consequently, the labour involved must have been very considerable.

The illustrations, of which there are no less than 676, with two coloured plates, play an important part; the reproductions

of the originals have been most faithfully carried out in the case of those taken from other sources, and of the drawings made especially we would note the series of sections made through the new-born medulla and stained with Weigert-Pal.

The great strides which have been made in the minute anatomy, owing to the improved methods of staining and the effect of this on the theory of the nervous system, are well shown by comparing this work with text-books of, say, ten years ago. There is probably no department of histology where the revolution has been so complete, and this difficult subject has been here treated in a most lucid and masterly fashion, and the result is a text-book, which workers in neurology on both sides of the Atlantic will find of the greatest help in ascertaining the latest views on the minute structure of the most complicated parts of the nervous system.

C. E. Beevor.

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*Semeiologie du Système Nerveux.* Par J. Dejerine, *professeur agrégé à la Faculté de Médecine de Paris, Médecin de la Salpêtrière.* (Paris: Masson et Cie. 18 francs).

This remarkable work forms the greater part of the fifth volume of the "Traité de Pathologie Générale," published by Professor Bouchard. It extends to eight hundred and twenty pages of text and contains three hundred and six illustrations. Its plan is a complete departure from the usual method of treating the diseases of the nervous system, for the author has limited himself entirely to the consideration and illustration of the symptomatology of the disorders of its various great functions.

The subject has been considered under the following heads: affections of intelligence; of speech; of the motor functions; of the sensory functions; of the reflexes; of the viscera, in so far as they are of nervous origin; of the trophic functions; and there is a special concluding chapter on the nervous affections of vision and the visual apparatus.

Under the disorders of intelligence are considered coma, sleep, insomnia, trance, somnambulism, ambulatory automatism, hypnotism and suggestion. Those affections which constitute insanity are beyond the scope of the work and are therefore not included.

The affections of speech are discussed under the heads of aphasia, dysarthria, mutism and stammering. The first of these, aphasia, is treated with great detail as to the differential diagnosis and localisation of its various forms and its progress. The author reiterates his views that there is no specialised graphic centre similar to the speech centre in Broca's convolution.

Nearly four hundred pages are devoted to the disorders of the motor functions, viz., paralyses, atrophy, ataxy, vertigo, contracture, convulsion, tremor, &c. There are special chapters on the anatomical localisation of the lesions which produce paralysis and muscular atrophies, and on the symptomatology of the hand, foot, face, attitude and gait, as well as on the mechanical and electrical reactions of nerves and muscles. This section of the work is a veritable storehouse of information on every disease and modification of the motor functions, and the illustrations, which are both numerous and apposite, are reproduced with a clearness that one has seldom, if ever, seen equalled.

The disorders of sensibility have been considered under the sections of superficial, deep and visceral sensibility, subjective disorders and localisation. Special attention is drawn to the investigation of the osseous sensibility and its relation to the deep reflexes—a relation which has been studied in Professor Dejerine's clinique by one of his pupils, but which does not yet appear to have attracted the attention which it deserves. A special chapter is devoted to the localisation of the lesions in the peripheral nerves, roots, cord and brain. The superficial and deep reflexes are discussed almost entirely from the clinical standpoint, as they are found in general diseases as well as in the organic and functional diseases of the nervous system. The relation of these reflexes to flaccid and rigid paralysis is more fully considered in the section on contracture (p. 265).

The visceral disorders (which are for the most part of a functional nature) and the trophic affections also receive adequate examination, as do the affections of the motor, sensory and central apparatus of vision.

The whole subject, thus hastily sketched, has been treated in a most masterly manner, with all the thoroughness, sense of proportion, and wealth of detail which Professor Dejerine's previous published work has led us to expect. The result is the production of a work which is at once unique and invaluable, not only to the student and teacher of nervous disease, but also to the busy general practitioner, who will find here, ready to hand, a series of clinical pictures of nervous diseases, such as are only to be found

together in large special hospitals, and he will also find, in a singularly clear and accessible form, most of the data for differential diagnosis. It is the most complete clinical encyclopædia of nervous diseases that has yet appeared in any language.

Of the illustrations which accompany the work it is difficult to speak in terms of sufficiently high praise. They are reproduced in a uniformly high standard of artistic excellence.

We trust that the work may be made accessible to a wider circle of readers in an English translation.

ALEXANDER BRUCE.

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*A Topographical Atlas of the Spinal Cord.* By ALEXANDER BRUCE, M.D. (Williams & Norgate, London and Edinburgh, 1901.)

IN the Atlas before us the author's aim has been to provide representations of sections which may be taken as typical of each of the segments of the spinal cord, with a view to determine the relative arrangement of the gray and white matter, especially the form of anterior horn characteristic of each segment; the relation and distribution of the motor nerve-cells; and any other features which may serve for the identification of the several segments. In this way a series of normal standards have been provided which will prove not only highly useful for the identification of sections submitted for examination, but will also serve as a basis of comparison with pathological conditions, and as an aid to the study of localisation of the motor functions of the spinal cord.

The determination of the exact locality of a given section of the cord may be made from the type of outline of the anterior horn, which is found to be constant for each segment or for corresponding parts of segments in different cords. It is only in the dorsal region, where the transition from segment to segment is less abrupt, that differentiation may become a matter of difficulty. The mesial column of cells persisting throughout the entire length of the cord, affords evidence that it supplies the muscles of the trunk; the lateral cell-columns being more closely related to the limb muscles. In the limb enlargements, the gray matter is increased by the accession of a promontory on its lateral aspect. It would appear also as if the groups of cells supplying the flexors of the limb were situated in the posterior part of the anterior horn, while those supplying the extensors lay in front. It is

probable also that there is some relation between the size of the motor cell and that of the muscular fibre which it innervates. This would explain the small size of the cells in the first dorsal segment, as compared with the rest of the cervical region.

The Atlas consists of thirty-two plates, one plate being given over to the delineation of a typical section from each of the segments of the cord. In the upper part of the plate there is a photograph of the arrangement of the cells of the anterior cornua, and in the lower a transverse section of the cord, giving the outline of the gray matter. A short description of the plate is found on the opposing page. The figures are photogravure reproductions of the original sections.

This Atlas is another instance of the careful and elaborate work which we associate with the name of the author.

W. A. Turner.

# PROCEEDINGS OF THE NEUROLOGICAL SOCIETY OF LONDON.

A PATHOLOGICAL MEETING was held at 11, Chandos Street, on Thursday, May 9, at 8.30 p.m., when the following communications were made:—

(I.) Dr. JOHN TURNER.—*A method of staining nervous tissues in methylene blue, whereby one is able to demonstrate:*

(1) The beaded network around the pyramidal nerve-cells and their processes;

(2) The "thorns" on the branches of Purkinje cells;

(3) And the basket-work around these latter.

The method appears to exert a selective influence in its action, staining some cells very darkly, others very lightly. The pyramidal and the Purkinje-cell systems stain light. The basket cells and small cortical cells of the cerebellum and certain small, square, pentagonal or pyriform cells of the cortex cerebri stain densely.

The staining appears to be permanent.

The drawbacks to it are that only parts of the tissue take on the stain. Neither the first layer of the cerebrum or the granular layer of the cerebellum stain.

Apparently it can only be got when the light and temperature are favourable, so that whilst in the spring, summer and early autumn successes are the rule, in the winter months and during cold dull weather they are the exception

(II.) Dr. MICHELL CLARKE.

(1) *Case of pachymeningitis of the spinal cord.*—From an agricultural labourer, aged 26. He had had rheumatic fever twice, had been much exposed to cold and damp, but denied syphilis. Duration of illness about eighteen months. Onset with weakness in legs, then shooting pains in arms, legs, and

trunk, tingling and numbness in legs, and some pain in back, with girdle pain about level of umbilicus. Gradual increase of paralysis in legs, with increase of deep reflexes, wasting of muscles, anæsthesia over certain areas, with patches of hyperæsthesia, and retention of urine.

Two months before death paralysis extended to upper extremities, with tingling and numbness, and shooting pains in them, followed by wasting of muscles. Later paresis of diaphragm.

For the last month almost total paralysis of limbs, with contraction and wasting. A marked clinical feature of the case was the extraordinary number of bedsores, which in spite of every precaution, formed on every bony point on which pressure occurred. There was disease of the mitral valve.

*Post mortem.*—The meninges covering the brain were normal. The ventricles, especially the lateral ventricles, were distended. The brain was rather small, but healthy in all parts.

*Spinal cord.*—Dura mater appeared normal externally, but on making transverse sections the cord was found to be enclosed from end to end in a dense fibrous envelope, measuring where thickest one-eighth of an inch in diameter. This envelope is formed partly of thickened dura mater, but chiefly of moderately dense newly formed connective tissue lying between the dura and the pia, which is also thickened. This new formation was thickest on the posterior aspect of the cord, and in the dorsal, upper lumbar and lower cervical regions, gradually ceasing at the upper cervical and sacral regions. The anterior and posterior nerve roots, and in parts most affected the posterior ganglia, were compressed and more or less destroyed; the outer margin of the cord to the extent of about one-eighth of an inch was destitute of nerve-fibres. The cord itself was compressed, its framework increased in density, and there was extensive atrophy of the cellular elements of the gray matter.

(2) *Changes in posterior columns of spinal cord in a case of pernicious anæmia.*—Sections show early stage of degeneration in posterior columns in cervical region (lower part chiefly) and cervico-dorsal region, not extending below second dorsal roots.

With the exception of slight tingling in hands and feet no symptoms of disease of the cord were present during life.

(3) *Tumour of the right optic thalamus*, involving the subthalamic region, and pressing on the right internal capsule; extending backwards it invaded the left subthalamic region, right

crusta, gray matter of origin of third nerves, and compressed the aqueduct of Sylvius. The corpora quadrigemina were flattened and displaced upwards.—Duration of illness two and a half years. Absence throughout of optic neuritis, vomiting and severe headache.

*Symptoms in order of onset.*—Diplopia, paresis left third nerve; paresis, burning pains, defective muscular sense and tactile sensation left arm and hand; horizontal nystagmus; paralysis left third nerve. *Very marked tremor, during movement only, of left upper extremity, exactly resembling tremor of disseminate sclerosis.* Speech deliberate. Want of variation in expression in features. Ptosis on both sides. Left hemianæsthesia. Left hemiplegia with exaggeration of deep reflexes.

Paralysis of both third and fourth nerves. Immobile dilated pupils. Finally paralysis on both sides of body, contracture, incontinence, drowsiness and coma.

(III.) Dr. WAKELIN BARRATT.—*Changes in the nervous system in a case of old-standing amputation.*

*Clinical account.*—Patient's upper limb was amputated at the middle of the upper arm when he was 19 years of age. He was in good health and led a very active life for thirty-six years afterwards. He then gradually became demented and died at the age of 61.

*Post-mortem appearances.*—There is hemiatrophy of the spinal cord on the side of the amputation in the whole length of the cervical region. In the medulla and pons there is atrophy of the pyramidal fibres of the opposite side. The hemiatrophy of the spinal cord affects both gray and white matter, the former showing diminution in number and size of the anterior horn cells.

There is little difference in the aspect of the posterior root ganglia on the two sides, nor is any striking change noticeable in the appearance of the nerve-roots, posterior and anterior, on the side of the amputation.

The brain is wasted and the pia-arachnoid at the vertex is opaque and thickened.

(IV.) Dr. FREDERICK BATTEN.—*Specimens from three cases of infantile paralysis.*

(1) Thirteen days after onset of disease.
(2) Three months after onset of disease.
(3) Two years after onset of disease.

AN EXTRAORDINARY MEETING was held in the Medical Department of the Owens College, Manchester, on the morning of June 22, 1901, when the following specimens were shown:—

Dr. A. BRUCE.—(1) Photogravures of each segment of the normal spinal cord. (2) Photographs and sections of: (*a*) Hæmorrhage into spinal cord. (*b*) Cavities in cord above a spina bifida. (*c*) Syringo-myelia. (*d*) Progressive muscular atrophy and amyotrophic lateral sclerosis. (*e*) Glioma of pons. (*f*) Syphilitic meningo-myelitis. (3) Photographs from a case of complete paralysis of the brachial plexus.

Dr. JUDSON BURY.—(1) Porencephalus. (2) Hydrocephalus. (3) Acromegaly.

Professor SHERIDAN DELÉPINE.—(1) Actinomycotic abscess of brain. (2) Experimental arsenical neuritis. (3) Other lesions of the central nervous system.

Professor J. DRESCHFELD.—(1) Spinal cord in ataxia paraplegia. (2) Spinal cord in disseminated myelitis. (3) Casts and photographs.

Mr. W. MILLIGAN.—(1) A portable surgical motor.

Dr. F. CRAVEN MOORE.—(1) Multiple gummata of brain and spinal cord. (2) Hæmorrhagic meningo-encephalitis (influenza). (Dr. Dreschfeld's case.) (3) Metastatic calcification of vastus internus tendon with Charcot's arthropathy. (Dr. Dreschfeld's case.) (4) Specimens from poisoning by arsenical beer. (5) Cerebral tumours.

Dr. F. W. MOTT.—(1) Effects of bitulin, abrin, absinthe, and picrotoxin upon nerve-cells.

Drs. ORR and ROWS.—(1) Types of nerve-cells in the spinal ganglia of rabbits. (2) Nerve-cells in the spinal ganglia of man and different forms of chromatolysis in general paralysis of the insane. (3) Spinal ganglion cells in acute mania, showing vacuolation.

Dr. E. S. REYNOLDS.—Photographs of neurological cases, including a series illustrative of the recent epidemic of arsenical poisoning.

Professor C. S. SHERRINGTON and Dr. E. E. LASLETT.—Microscopical sections (*infra*).

Professor W. STIRLING.—(1) Exhibits to illustrate some of the phenomena of stereoscopic vision. (2) An original experiment on binocular colour vision. (3) An experiment to show how the actual size of the pupil is affected by the cornea. (4) View of the interior of the frog's heart to show the arrangement of its muscular fibres. (5) Enucleation of the eyeball and removal of the floor of the orbital cavity, showing position of soft palate in phonation. (6) Simple method of examining the retina in a living rabbit. (7) A classical experiment concerning the discovery of the capillaries (Malpighi, de pulmonibus) and a modern one. (8) Some optical illusions. (9) Some experiments in physiological optics. (10) Lantern slides of some distinguished physiologists. (11) Original picture of the Kircher's "Experimentum Mirabile." (12) Some anaglyphs. (13) The structure of some electrical organs. (14) Complete injection of the blood-vessels of the eyeball of a small animal.

Dr. E. F. TREVELYAN.—(1) Various specimens showing the value and permanency of Laskowsky's method. (2) Specimens preserved in Kaiserling's fluid. (3) Tuberculous tumour of the brain, meninges and skull. (4) Intact pia-arachnoid from a fœtus.

Prof. A. H. YOUNG.—Stereoscopic photographs of the brain.

Dr. W. B. WARRINGTON.—(1) Sections of unilateral atrophy. (2) Photographs of Tooth's peroneal atrophy.

Dr. R. T. WILLIAMSON.—(1) Two cerebellar tumours with photographs. (2) Microscopical specimens of:—(*a*) Progressive muscular atrophy. (*b*) Early tabes. (*c*) Acute anterior poliomyelitis of the adult. (*d*) Myelitis in the distribution of the anterior and of the posterior spinal arteries. (*e*) Peripheral nerves in multiple neuritis. (*f*) Spinal syphilis—thrombosis, hæmorrhage and myelitis. (*g*) Retro-bulbar optic neuritis associated with cancer of stomach.

*Clinical cases were shown by :—*

Dr. ASHBY.

Dr. JUDSON S. BURY.—(1) Syringomyelia with hemianæsthesia. (2) Sensory aphasia (two cases). (3) Ophthalmoplegia. (4) Hemiplegia, hemianæsthesia and impairment of special senses on one side. (5) Cases of muscular atrophy. (6) Hæmorrhage (?) into the spinal cord.

Dr. DRESCHFELD.—(1) Thomsen's disease (two cases). (2) A family (five cases) showing various stages of Erb's muscular dystrophy.

Dr. HARING.

Dr. HARRIS.—Unusual defect in the skull (? cephalhydrocele) with both hysterical and epileptic attacks.

Dr. DIXON MANN.

Dr. E. S. REYNOLDS.—(1) Locomotor ataxia with multiple joint lesions. (2) Unilateral lesion of the spinal cord (two cases). (3) Ataxia paraplegia (disseminated sclerosis?). (4) Chronic anterior polio-myelitis.

Dr. R. T. WILLIAMSON.—(1) Unilateral tremor most marked in leg (? paralysis agitans). (2) Very early tabes with knee-jerks present (two cases). (3) Disseminated sclerosis following influenza.

Dr. WILLIAMSON and Dr. P. TYTLER.—Hydatid of spine (extra-dural) with compression myelitis. Operation with gradual improvement for twelve months.

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Prof. C. S. SHERRINGTON and Dr. E. E. LASLETT gave a short "note on the third, fourth and sixth cranial nerves."

Drs. ALEXANDER BRUCE, MOTT and ORR gave lantern demonstrations of specimens shown in the Histological Laboratory (*supra*).

Prof. WM. STIRLING showed (1) Some classical experiments bearing on neuro-physiology, and one new experiment. (2) Malapterurus electricus (living) and its mode of feeding.